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TREATMENT OF THYROTOXICOSIS WITH RADIOACTIVE IODINE (I^{131}).

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RADIOIODINE (I^{130}) was first used in the treatment of toxic goitre at the Massachusetts General Hospital on January 21, 1941, and I^{131} became available there in August, 1946. Since then, results in thousands of cases of thyrotoxicosis treated with I^{131} have been published. A review of this therapy over a decade was reported by Chapman and Maloof (1955).

In Australia, recognition of the value of I^{131} in the treatment of thyrotoxicosis has generally been tardy. Since 1950 at the Royal Melbourne Hospital, members of the Thyroid Panel, the composition of which has varied somewhat, have investigated this subject. The chief difficulty in the use of I^{131} is the estimation of the requisite dose. Various methods of estimating dosage were tried in this clinic. Originally a groundless fear of deleterious effects kept the dosage, estimated at 6000 equivalent *r*, too low, hence treatment was unduly prolonged (Madigan and King, 1954).

In March, 1953, a simple method of estimating the dose was introduced, and it has proved satisfactory for treating patients as far away as Perth on advice from Melbourne. Its use should therefore make this therapy potentially available to the practitioner in the outback. A preliminary report of results in 33 cases was given by Fairley (1954). Two of the 22 patients with diffuse toxic goitre had previously received treatment with small doses of I^{131} and became hypothyroid with further therapy; their inclusion resulted in an unduly high incidence of hypothyroidism, and they are excluded from the present series. The other 31, including five with post-operative recurrence of thyrotoxicosis and six with nodular toxic goitre, practically all followed for a longer period, are included in this report.

Results of treatment are considered under the following headings: (i) diffuse toxic goitre, (ii) post-operative recurrent diffuse toxic goitre, (iii) nodular toxic goitre. The same criteria were used in estimating the required dose in all groups; but this dosage is far too small for nodular toxic goitres, for which operation remains the treatment of choice. Treatment with I^{131} is replacing operation in the other two groups.

[1] The Thyroid Panel, over the period covered by this paper, included, in addition to the authors, Miss E. V. Sherriff, of the Commonwealth X-Ray and Radium Laboratory, University of Melbourne, and Mrs. D. Winikoff, of the Department of Biochemistry, University of Melbourne.

The Estimation of the Requisite Dose of I^{131}.

Initially seven millicuries of I^{131} were taken as the "basic" dose for a patient with a thyroid gland of moderate (two to three times the normal) size, with a moderate (average) degree of hyperthyroidism, and with a retention of from 55% to under 70% of a tracer dose of 20 microcuries of I^{131} given orally twenty-four hours previously. In September, 1954, the basic dose was changed to six millicuries; but, as will be shown later, this was much less satisfactory. Modifications of the basic dose were made for the following factors: (i) the size of the gland, (ii) the degree of thyrotoxicosis, (iii) the degree of iodine retention by the goitre as shown by tracer tests. In practically every case in which the dose was altered for any other reason—that is, for age (a reduction because a patient was in her "teens") or for gross exophthalmos (a reduction because ensuing hypothyroidism might make the exophthalmos worse), such alteration proved to be wrong.

The Size of the Thyroid Gland.

Overseas observers have attempted to estimate the weight of the gland by various means, all more or less inaccurate. This proved unsatisfactory here, and the simpler method of estimating that the goitre was of the moderate size found in the usual case of toxic goitre, or was larger or smaller than this, was adopted. If the gland was of moderate size (about two to three times the normal size) no change in dosage was made; if it was decidedly smaller than this, one millicurie was subtracted from the basic dose; if it was appreciably larger one millicurie, and if it was very large two millicuries were added to the basic dose. This proved to be a most important factor in estimating the correct dose.

The Degree of Thyrotoxicosis.

When the hyperthyroidism was of moderate severity no change in dosage was made. With more severe hyperthyroidism, greater hyperplasia of the thyroid cells would presumably be present, and these younger cells would be more sensitive to radiation therapy. Hence, in contradistinction to many workers, including Blomfield *et alii* (1955), who increased the dose under these circumstances, presumably because of the more rapid turnover of I^{131} by the thyroid, one millicurie was subtracted from the basic dose of I^{131} for hyperthyroidism of greater than average severity. When the degree of hyperthyroidism seemed to be less than average, one millicurie was added to the basic dose; but often previous treatment had controlled the thyrotoxicosis, so that an accurate estimation of the degree of hyperthyroidism due to the pathological process itself was difficult. Alterations in dosage for thyrotoxicosis of varying severity were seldom made, and generally were not of great value, and this factor is no longer used in estimating the requisite dose. Blomfield *et alii* (1955) also now use only the size of the gland and the uptake of iodine by the goitre in calculating the dose, though their method of calculation is more involved than that recommended here.

Retention of I^{131} by the Thyroid Gland Twenty-Four Hours after Ingestion of a Tracer Dose of 20 Microcuries of I^{131}.

Most patients with toxic goitres retain 70% or more of a tracer dose of I^{131} at the end of twenty-four hours. With such a high retention, radiation effects will naturally be greater than with a lower retention, which is found in a few cases of toxic goitre and also usually in patients without thyrotoxicosis. In the latter group the lower retention of I^{131} tends to minimize the ill effects of treatment by I^{131} in any patient in whom an incorrect diagnosis of thyrotoxicosis has been made.

Adjustments of dosage according to results of tracer tests were to subtract one millicurie from the basic dose when the retention of iodine was 70% or more, and to make no change for retention from 55% to less than 70%, while one millicurie was added when the figure was less than 55%. This was an important factor (when available) in adjusting dosage, though, as will be shown later, modifications are needed in the foregoing figures. Moreover, patients can be treated satisfactorily with I^{131} without the help of this retention factor.

Diffuse Toxic Goitre.

Sixty-four patients with diffuse toxic goitre who had not previously received any therapy with I^{131} were treated. In 32 cases the basic dose of I^{131} was seven millicuries and in the other 32 it was six millicuries.

Patients Treated with I^{131} Without the Aid of Tracer Tests.

For various reasons, in 21 of these 64 cases no tracer tests were made, the basic dose being adjusted only on clinical observations of the size of the gland and the degree of toxicity. The results of treatment of these patients are shown in Table I.

Table I.

Results of Treatment of Diffuse Toxic Goitre with a Single Dose of I^{131} when Tests for Retention of a Tracer Dose of I^{131} by the Thyroid Gland were not Performed.

Basic Dose of I^{131}. (Millicuries.)	Number of Cases.	Size of Thyroid Gland.		Functional State of Thyroid Gland.		
		Normal.	Enlarged.	Euthyroidism.	Hypothyroidism.	Hyperthyroidism.
7	13	13	0	12	1[1]	0
6	8	5	3[2]	5	0	3[2]

[1] This patient requires one grain of thyroid daily to remain euthyroid.

[2] For various reasons, all three patients received one millicurie less than the calculated dose.

It is seen from Table I that, in the 13 cases in which the basic dose was seven millicuries, results were excellent. In every case the gland became normal in size, though one patient subsequently, when lactating, had a gland about twice the normal size. All patients except one became euthyroid. In the one exception (Case 6, Miss A.), the calculated dose of seven millicuries was reduced by one millicurie because, prior to the use of I^{131}, hypothyroidism was readily induced by methylthiouracil, but any attempt to reduce the dose resulted in hyperthyroidism. The assumption that hypothyroidism would be induced more readily than in the average case proved correct, and the patient remains euthyroid on a dosage of one grain of thyroid daily. One patient received five millicuries of I^{131}, six patients were given six millicuries, five received seven millicuries, and one was given eight millicuries.

When the basic dose was six millicuries of I^{131}, five of the eight patients obtained perfect results, three receiving five millicuries, while two were given six millicuries. In the other three, each of whom received one millicurie less than the calculated dose for various reasons, hyperthyroidism persisted with enlargement of the thyroid gland. One received five millicuries of I^{131} and two were given six millicuries. Two recently received a second dose of I^{131}. In the third case (Case 63, Mrs. B.), because malignant exophthalmos was present, the calculated dose of seven millicuries was reduced to six millicuries to avoid possible hypothyroidism which might increase the exophthalmos. A fortnight later a tarsorrhaphy and a transfrontal orbital decompression were performed on each eye. Six months later the thyroid gland was about twice the normal size, and the persistent thyrotoxicosis was controlled by "Neo-mercazole", which was considered preferable to another dose of I^{131} because of the possibility of inducing permanent hypothyroidism with I^{131}.

Adjustment of the Dose of I^{131} for the Size of the Goitre and the Severity of the Hyperthyroidism.

Many factors influence the ultimate result of treatment of thyrotoxicosis by I^{131}. When several variables are used in estimating dosage, and when other factors, such as the

possible subsequent use of antithyroid drugs over some weeks or months, may affect the result, it is difficult to evaluate the part played by any individual factor. However, in six of these 21 cases the sole alteration of the basic dose was a reduction of one millicurie for a goitre of less than moderate size, and in every case the result was excellent. Three patients received no antithyroid drugs; the other three were given them for one, three and five weeks subsequently. Likewise, excellent results were obtained in three cases in which the only alteration in the basic dose was a reduction of one millicurie for severe thyrotoxicosis, although two patients received antithyroid drugs for nearly three months and the other for a few weeks after I^{131} was given. Apparently these adjustments of the basic dose according to the size of the gland and the degree of hyperthyroidism were of value in estimating the correct dose of I^{131} for these patients.

TABLE II.

Treatment of Diffuse Toxic Goitre with a Single Oral Dose of I^{131}. Results in Relation to Dosage when Tracer Tests were not Available.

Results.	Dosage in Millicuries.				Total.
	5	6	7	8	
Excellent	4	7	5	1	17
Hypothyroidism	—	1	—	—	1
Persistent goitre with hyperthyroidism	1[1]	2[1]	—	—	3[1]
Total	5	10	5	1	21

[1] These patients received one millicurie less than the calculated dose of I^{131}, the basic dose being six millicuries.

When results of treatment are considered in relation to the dose of I^{131} given, as shown in Table II, it is seen that the majority of patients received six millicuries, but the best results were obtained with a dose of seven millicuries. All four patients with unsatisfactory results received one millicurie less than the calculated dose. The case of hypothyroidism (Case 6, mentioned above) is the only one of these 92 cases in which an alteration of the dose for factors other than the size of the gland, the degree of toxicity and the retention of iodine by the goitre proved to be correct. Had this patient received the calculated dose of seven millicuries, the resultant hypothyroidism would have been more severe.

These results show that satisfactory treatment of diffuse toxic goitre with I^{131} is possible without the use of tracer tests to determine the retention of I^{131} by the thyroid gland. In this small series the results were better in the group in which tracer tests were not utilized (Table III). A basic dose of seven millicuries gave better results than one of six millicuries when appropriate adjustments of the dose were made for the size of the thyroid gland and the severity of the thyrotoxicosis.

Results of Treatment of Diffuse Toxic Goitre by the Use of a "Basic" Dose of Seven Millicuries of I^{131}.

Table III shows the results of a single oral dose of I^{131} in 32 patients with diffuse toxic goitre when a basic dose of seven millicuries was used.

Persistent Enlargement of the Thyroid Gland after I^{131} Therapy.

The most unsatisfactory feature shown in Table III is the high incidence of persistent thyroid enlargement. However, this is not of much significance, since in two patients the gland is only about twice the normal size and is barely visible, in one it is about three times, and in one about four times the size of the normal gland. Only in the last patient is the goitre very obvious. These four are euthyroid and are among the five patients with the lowest retention of iodine in this group of 19 patients. In the other case (Case 43, Mrs. C.) in which there was only 11% retention (probably due to prior ingestion of iodine in some unrecognized form), fourteen months elapsed before the gland reverted to normal size after a dose of nine millicuries of I^{131}. The calculated dose of 10 millicuries was reduced by one millicurie because the patient was thought to have been hypothyroid before the onset of the hyperthyroidism, and such patients usually respond readily to other methods of medical treatment. It is in patients with unusually low retention of iodine by the thyroid gland that tracer tests are of the greatest value. The histories of these four patients are given briefly as follows.

TABLE III.

Therapeutic Results from a Single Oral Dose of I^{131} in Diffuse Toxic Goitre, the "Basic" Dose being Seven Millicuries.

Tracer Tests.	Number of Cases.	Size of Thyroid Gland.		Functional State of Thyroid Gland.	
		Normal.	Enlarged.	Euthyroid.	Hypothyroid.
Available	19	15	4	18	1
Not performed	13	13	—	12	1
Total	32	28	4	30	2

CASE 9.—Mrs. D. was known to have had a goitre for thirty years. Treatment with antithyroid drugs and iodine for seven months before she was examined was unsuccessful, but this use of iodine accounted for the retention of only 9% of the tracer dose. After nine millicuries of I^{131} had been given, the thyrotoxicosis was controlled; but twenty months later the gland was still about three times the normal size.

CASE 15.—Mrs. E. became approximately euthyroid on "Neo-mercazole" treatment, given for a month before treatment with I^{131}, but the gland increased in size. The retention of I^{131} was 48%. The calculated dose was nine millicuries, but only eight millicuries were given. During the next fortnight "Neo-mercazole" treatment was continued and the goitre became larger. This drug was then omitted, but the gland was still about twice the normal size ten months later, though the circumference of the neck was 4·7 centimetres (nearly two inches) smaller. If the full calculated dose of nine millicuries had been given and subsequently "Neo-mercazole" treatment had not been continued unnecessarily, the gland almost certainly would have returned to normal size.

CASE 42.—Mrs. F., with a retention of only 38·5% of iodine for no obvious reason, became euthyroid after a dose of eight millicuries of I^{131}, but a year later the gland was still about twice the normal size.

CASE 34.—In Mrs. G., the only patient with a really unsatisfactory result, the retention of I^{131} was 55%. After a dose of seven millicuries of I^{131}, methylthiouracil was given for a month, followed by deep X-ray therapy to the retroorbital tissues because of gross exophthalmos. Three months after taking I^{131} she was euthyroid, but the goitre was large. Another course of deep X-ray therapy and a small dose of thyroid were prescribed for the exophthalmos, but the thyroid was soon omitted because of nervous upset. Eight months after the dose of I^{131}, the protein-bound iodine content of the blood was 3·9γ per 100 millilitres (normal figures are between 3·0 and 7·5γ). A month later pretibial myxœdema developed and stilbœstrol and thyroid were given, but the latter again had to be omitted because of nervous symptoms. Twenty months after treatment with I^{131}, the thyroid gland was still about four times its normal size. No satisfactory reason can be advanced to account for this persistent thyroid enlargement.

Because these four patients with persistent goitres all showed low or relatively low retention of I^{131} by the thyroid gland following a tracer test, finer adjustments of the dose in relation to this factor than were used in this series are obviously indicated, and in this clinic the following adjustments are now used. With retention of 70% or more of the tracer dose, the basic dose of I^{131} is reduced by one millicurie; with retention from 60% to less than

70%, no change is made; from 50% to less than 60% one millicurie, and from 40% to less than 50% two millicuries are added to the basic dose of seven millicuries.

When the retention of a tracer dose is less than 40%, treatment with I^{131} is postponed for some weeks and care is taken to avoid any extra intake of iodine. The use of a diet low in iodine is valuable. Thyrotoxicosis may be controlled over this period with antithyroid drugs. However, it is unnecessary to omit the ingestion of thyroid if it is indicated, since Greer and Smith (1954) found that 55 patients with non-toxic goitres all had twenty-four hour retention figures of less than 20% after taking from three to nine grains of thyroid daily for one or two weeks, while in 23 patients with thyrotoxicosis there was no appreciable suppression of retention of I^{131} even after 12 grains of thyroid had been taken daily for this period, and in only one of these was the retention below 20%. They suggest that this failure of large doses of thyroid to lower the retention of iodine by the thyroid gland in thyrotoxicosis is a valuable diagnostic test in doubtful cases.

Sherriff (1956), in this clinic, has shown that antithyroid drugs need not be omitted for longer than twenty-eight hours before I^{131} is given, and if necessary they may be resumed forty-eight hours after the dose of I^{131}. The following history illustrates the value of omitting the antithyroid drug twenty-eight hours before the I^{131} is given.

CASE 56.—Mr. H., aged fifty-six years, presented on November 29, 1954, with a small diffuse toxic goitre, auricular fibrillation, and congestive cardiac failure. There was a systolic thrill with a harsh systolic bruit maximal over the third left intercostal space. Thyrotoxicosis had been present for at least six months. A tracer test on December 1 showed a retention of 45%, but orders to omit "Neo-mercazole" twenty-eight hours before the test had not been carried out. At 6 a.m. on December 5 the last dose of "Neo-mercazole" was taken before the tracer test was repeated at 10 a.m. on the next day, when the retention of I^{131}, five days after the previous test, was 80%. Because of persistent auricular fibrillation, "Neo-mercazole" was continued for nearly six months after five millicuries of I^{131} had been given on December 15. On June 10, 1955, he was euthyroid, but the thyroid gland was larger than before the I^{131} was given.

There is a latent period, usually of about six weeks, after I^{131} is given before its effects become manifest. Over this time, if the patient has auricular fibrillation or severe thyrotoxicosis, antithyroid drugs may be given in appropriate dosage unless there is some contraindication to their use. But after six weeks they should be omitted, so that the effect of the I^{131}, which will be nearing its maximum in another month, can be estimated. Chapman and Maloof (1955) avoid using these drugs after I^{131} if possible. If they are given in excessive doses or if their use is unduly prolonged, temporary hypothyroidism and enlargement of the goitre are likely to result, and this enlargement may take many months to subside. When the gland is initially decidedly larger than in the average case, it is much easier with I^{131} to control the thyrotoxicosis than to reduce the gland to normal size. In such patients only small doses of antithyroid drugs should be continued for a limited period after I^{131} has been given. The result of incorrect use of an antithyroid drug is shown in the following history.

CASE 3.—Mrs. I., aged twenty-two years, on October 24, 1952, gave a history of a goitre present for several years with toxic manifestations for a year. After a fortnight of methylthiouracil therapy, this was omitted for three days before 6·2 millicuries of I^{131} were given on November 14, and then was continued till April 19, 1953, when the goitre was larger and mild hypothyroidism was present, which subsequently rapidly subsided without thyroid therapy. On June 12 she was euthyroid, and a proposal of operation on the unsightly goitre was rejected, since hypothyroidism would certainly have resulted. One month later this large goitre had almost disappeared, and on September 11 the thyroid gland was barely palpable. When she was discharged from the clinic on September 10, 1954, she was euthyroid and the thyroid gland could not be felt.

In this case unduly prolonged use of methylthiouracil led to an increase in the size of the goitre and temporary hypothyroidism. For at least two months after the drug had been omitted, the goitre remained unchanged and then rapidly decreased in size over three to four weeks. Complete cure eventually resulted without any other treatment, although it took nearly five months for the gland to reach normal dimensions.

Iodine is still frequently administered to patients with thyrotoxicosis, usually with antithyroid drugs, but occasionally alone. The previous use of iodine interferes much more with the retention of I^{131} by the thyroid than does the use of antithyroid drugs. The prior ingestion of such drugs makes the diagnosis of thyrotoxicosis more difficult for the consultant, though their diagnostic value in therapeutic tests is often very great. When I^{131} is to be given, antithyroid drugs are preferred to iodine, should immediate treatment be necessary. If this is unnecessary, it is better to refer the patient without prescribing these drugs or iodine, since they make the estimation of the serum protein-bound iodine useless as a test of thyroid function for several weeks at least. Likewise when iodine has been taken, usually several weeks must elapse after it has been omitted before therapy with I^{131} can be satisfactorily given, and preferably this should be postponed until the tracer test shows that the retention of I^{131} by the thyroid has risen to 60% or more.

Hypothyroidism after I^{131} Therapy.

One of the 19 patients on whom retention tests were performed became permanently hypothyroid (Table III), and her history is now given.

CASE 40.—Mrs. J., aged forty-four years, was referred by Dr. R. Kaye Scott on July 30, 1954, with the history of incomplete surgical removal in June, 1952, of an adenocarcinoma of the fundus of the uterus, infiltrating widely through the left ovary and broad ligament. Courses of deep X-ray therapy to the pelvis were given in July and December, 1952. In March, 1953, a colostomy was established for a recto-vaginal fistula. A goitre was first noticed in January, 1954, and later exophthalmos developed.

On August 11, 1954, seven millicuries of I^{131} were given for a diffuse, mildly toxic goitre of moderate size, with a retention of 70% of the tracer dose. On October 22 the patient complained of being sluggish and had puffy eyelids, a dry, cool skin and a blood pressure of 210 millimetres of mercury, systolic, and 120 millimetres, diastolic; the corresponding figures before treatment were 170 and 90 millimetres of mercury. One grain of thyroid daily was of little benefit, and on February 18, 1955, because of loss of hair and other symptoms, the dose was increased to two grains and, on April 15 to three grains daily. A month later she was "amazed" at how thickly her hair had grown. Slight nocturnal palpitation and hot flushes were rapidly relieved by stilbœstrol. On July 15 the size of the thyroid was normal, she was euthyroid on a dosage of three grains of thyroid daily, and the blood pressure was 170 millimetres of mercury, systolic, and 105 millimetres, diastolic. In January, 1956, diplopia had appeared. On July 10, 1956, mild hypothyroidism was obviously due to a reduction of the dose of thyroid (because the supply of tablets was running out). The thyroid was not palpable and diplopia was less pronounced. The blood pressure had risen again to 210 millimetres of mercury, systolic, and 120 millimetres, diastolic.

Temporary hypothyroidism is not uncommon from four to nine months after I^{131} therapy, as is illustrated in the following history.

CASE 10.—Mrs. K., who had previously been treated with methylthiouracil for a year, had relapsed when the drug was omitted. Five months after she took six millicuries of I^{131}, the thyroid was not palpable, the hands were dry and the blood pressure was 170 millimetres of mercury, systolic, and 110 millimetres, diastolic (the corresponding figures before treatment were 180 and 80 millimetres). Two months later many of the classical signs of hypothyroidism were obvious. After a month on a dosage of one grain of thyroid daily, the blood pressure was 180 millimetres of mercury, systolic, and 100 millimetres, diastolic. When she was last examined a year after taking the I^{131}, she complained of various aches and of a large lump in the neck, which was normal when examined. This history records that she was "always full of moans". She was still taking one grain of thyroid daily, but this was omitted, since it appeared that her hypothyroidism was temporary and that the present complaints were of nervous origin.

These two patients show an important sign noted in several others with temporary or permanent hypo-

thyroidism—namely, a rise in the diastolic blood pressure, which is a frequent early sign in patients developing hypothyroidism, and sometimes may be the first sign to suggest this complication.

Results of Alteration of the Basic Dose of I^{131} by Various Factors.

Of these 32 patients, three, none of whom subsequently received antithyroid drugs, were given an extra one millicurie of I^{131} because of a mild degree of hyperthyroidism (less than average). The results were excellent in the two cases in which this was the sole adjustment of the basic dose. The other patient (Case 40), whose history has just been given, became hypothyroid despite the subtraction of one millicurie from the dose because of high iodine retention by the goitre. It is difficult to determine the degree of hyperthyroidism due to the disease when other factors such as antithyroid drugs have been exerting their influence. Little would have been lost in this series if this factor of toxicity had been neglected in estimating the dose required; its use has since been abandoned.

In nine cases the basic dose was increased because of the large size of the goitre, with excellent results in seven. In the other two in which the dose was increased further because of low retention of iodine by the goitre, the thyrotoxicosis was abolished, but the thyroid remained enlarged. Of the seven cases in which excellent results were obtained, the dose was reduced in five because of high iodine retention, and in four because of severe hyperthyroidism.

In summary, when seven millicuries of I^{131} are taken as the basic dose and appropriate adjustments are made for the size of the gland, for the severity of the hyperthyroidism and for the degree of retention of iodine by the thyroid gland when this is known, especially when the retention is unduly low, excellent results are obtained in the treatment of diffuse toxic goitre with I^{131}. In only one of these 32 patients is the result really unsatisfactory; this is the patient with the very obvious persistent goitre (about four times the size of the normal gland), and this result is unsatisfactory only from the æsthetic viewpoint. The one patient with permanent hypothyroidism is in normal health and is perfectly satisfied with the result while taking three grains of thyroid once a day.

Results of Treatment of Diffuse Toxic Goitre when the Basic Dose of I^{131} was Six Millicuries.

In Table IV is given an analysis of the much less satisfactory results in 32 cases of diffuse toxic goitre treated with I^{131} when a basic dose of six millicuries was used. The eight cases in which retention tests were not performed have already been discussed (Table I).

TABLE IV.

Therapeutic Results from a Single Oral Dose of I^{131} in Diffuse Toxic Goitre, the Basic Dose being Six Millicuries.

Tracer Tests.	Number of Cases.	Size of Thyroid Gland.		Functional State of Thyroid Gland.		
		Normal.	Enlarged.	Euthyroid.	Hypothyroid.	Hyperthyroid.
Available	24	11	13	20	1	3
Not performed..	8	5	3	5	—	3
Total	32	16	16	25	1	6

Hypothyroidism.

The history of the only one of these 32 patients who developed hypothyroidism is of interest.

CASE 31.—Mrs. L. gave a story suggesting that thyrotoxicosis had arisen eight months earlier, but in the two months before she was examined there had been an increase of 10 pounds in weight. This followed a loss of 32 pounds in the preceding six months despite a good appetite. The thyroid gland was slightly enlarged, the clinical diagnosis was doubtful as to the presence of thyrotoxicosis, the retention of I^{131} by the thyroid gland was 76% and the protein-bound iodine content of the serum was 12·9γ per 100 millilitres. This last result was almost certainly incorrectly interpreted as indicating thyrotoxicosis; the high value was probably due to a cholecystographic examination carried out two months previously. On December 17, 1954, four millicuries of I^{131} (the smallest dose used in this series) were given. Four months later an increase in weight and loss of energy were noted. On June 4, 1955, the skin was dry, the eyebrows were thin and periorbital puffiness was present. When the patient was last examined on September 2, 1955, she was apparently euthyroid on a dose of 1·5 grains of thyroid daily.

This hypothyroidism may yet prove to be temporary. If thyrotoxicosis had ever been present, a remission had apparently occurred before the I^{131} was given. Permanent hypothyroidism is obviously uncommon when a basic dose of six millicuries of I^{131} is used in treatment of diffuse toxic goitre.

Persistent Hyperthyroidism.

Of the 24 patients subjected to tracer tests (Table V), three whose histories are given and who each received five millicuries of I^{131} showed persistence or recurrence of both the goitre and the hyperthyroidism, and were given a second dose of I^{131}.

CASE 58.—Mrs. M. was euthyroid for some months after the gland had been reduced to about one and a half times the normal size, but gross exophthalmos persisted. Eleven months after the initial dose of I^{131}, thyrotoxicosis recurred. A month later, on November 16, 1955, she received four millicuries of I^{131}, the dose being kept low to avoid any increase in the exophthalmos which might result if hypothyroidism ensued. On July 11, 1956, the exophthalmos had decreased slightly, she was euthyroid, and the left lobe and isthmus of the gland were very slightly larger than normal.

CASE 64.—Mrs. N. received five millicuries instead of six millicuries of I^{131} on November 8, 1954. An isolated attack of typical tetany, rapidly relieved by calcium gluconate given intravenously, occurred on March 15, 1955, in association with a gastro-intestinal infection. From February, 1955, she was otherwise well, but in August thyrotoxicosis recurred. On September 20, 1955, a second dose of five millicuries of I^{131} was given. Five months later she was euthyroid, but the gland still remained from two to three times the normal size. On July 4, 1956, it was smaller, but its size was not defined.

CASE 32.—Miss O., on May 25, 1955, received five millicuries of I^{131}, with no apparent effect whatever over the next six months. There was no history of the dose having been vomited and no obvious reason for this unique absence of any therapeutic effect. Another dose of five millicuries was given on November 16, 1955. On May 16, 1956, she was euthyroid, and the thyroid gland was about one and a half times the normal size.

In these three cases of persistent or recurrent hyperthyroidism the initial dose of I^{131} was obviously too low.

Persistent Enlargement of the Thyroid Gland.

The most unsatisfactory feature of these 24 cases in which tracer doses of I^{131} were given is the persistence of the goitre in 13 of them, including the three just considered in which there was persistent or recurrent thyrotoxicosis. The other 10 patients were euthyroid, and in two of these cases the calculated dose was reduced by one millicurie. In one this was done because of gross exophthalmos, and seven months after a dose of five millicuries the gland was still about twice the normal size. In the other, the dose was reduced to four millicuries because the patient was only sixteen years old, and "Neo-mercazole" was given for the next six weeks. Seven months later the goitre was about four times the size of the normal gland. Almost always, attempts to adjust the dose of I^{131} because of factors other than the three usually applied proved to be wrong.

In another two patients who received five millicuries of I^{131} the gland was only about one and a half times the normal size. One contracted infectious hepatitis five months after this therapy and was last examined two months later. The other took "Neo-mercazole" for fifteen weeks after the I^{131} and was last examined eight months later.

In three cases the gland was about two to three times the normal size, two patients being last examined seven months after I^{131} had been given. One received no antithyroid drugs after a dose of five millicuries, the other had taken methylthiouracil for fourteen weeks after a dose of seven millicuries of I^{131}. The third patient had taken methylthiouracil for thirteen weeks after receiving six millicuries of I^{131}, during which time the goitre increased to about six times the normal size. Eleven weeks after the drug had been omitted, the gland had decreased to about half this size without any other treatment.

The history of Mr. H. (Case 56) has already been given. While "Neo-mercazole" was taken for six months after a dose of five millicuries of I^{131} the gland increased in size and auricular fibrillation persisted. Another patient who took "Neo-mercazole" for seven weeks after a dose of five millicuries of I^{131} still had an enlarged gland nine weeks after the drug had been omitted. In these two cases there is no note of the approximate size of the gland.

The history of the last patient is given in more detail, since it illustrates common faults in the management of these cases.

CASE 71.—Miss P., aged fifty years, was first examined on March 25, 1955, with a history of goitre present for fifteen months and of thyrotoxicosis of three months' duration. During six weeks of iodine therapy there had been general improvement and the gland had decreased in size, but she had felt worse after the iodine had been omitted for a fortnight. Iodine and methylthiouracil had then been given for two weeks until March 9. The ingestion of iodine prevented the protein-bound iodine estimation being reliable and led to low retention of I^{131} in the thyroid gland at twenty-four hours, the results being 28% on March 30 and 27% on April 19. It would have been better to postpone giving I^{131} for some weeks, continuing treatment if necessary with methylthiouracil only and omitting the iodine, until the retention of iodine by the thyroid had increased if possible to at least 60%. However, two millicuries were added to the dose because of the low retention, and on April 20 eight millicuries of I^{131} were given. The administration of methylthiouracil was continued for the next four months, during which time the thyroid increased in size. On September 16 the gland was about three times the normal size, and on November 11 the gland was still "moderately enlarged", although the patient was euthyroid.

This history illustrates the disadvantage of the administration of iodine in any form within a few weeks of I^{131} therapy. This drug also renders the estimation of protein-bound iodine valueless for some weeks as a test for thyroid function. The deleterious effect of excessively prolonged therapy with antithyroid drugs is also illustrated.

In this group the persistent enlargement of the thyroid gland is related to the following two factors:

1. Insufficient dosage in all cases. A basic dose of six millicuries is obviously too low to be satisfactory. In two patients the extraneous factors of age and gross exophthalmos were wrongly considered to be indications for a further reduction of dosage.

2. Unduly prolonged and excessive therapy with antithyroid drugs. This was an important factor in at least five of these cases. These drugs should only rarely be used for more than six weeks after I^{131} is given. They are better avoided altogether at this stage unless the hyperthyroidism is severe.

THE VALUE OF TRACER TESTS TO DETERMINE THE RETENTION OF I^{131} BY THE THYROID GLAND.

Of the 64 patients with diffuse toxic goitre, 43 were subjected to tracer tests. In 32 there was a retention of 70% or more of the dose of I^{131} by the thyroid gland at the end of twenty-four hours, and one millicurie was subtracted from the basic dose in these cases. No change in dosage was made for retention ranging from 55% to less than 70% in four patients. In seven cases less than 55% of the tracer dose was retained, the figures being 9%, 11%, 27%, 38·5%, 48%, 51% and 54%. The addition of one millicurie to the basic dose in these cases was correct so far as it went; but in those patients with a retention of less than 50% there was a great tendency for the gland to remain enlarged, and, as has been mentioned previously, a more delicate adjustment of the dosage in relation to these lower figures has now been instituted. The chief value of the tracer test is in the recognition of this group with relatively low retention of iodine by the goitre.

Results in Relation to the Dosage of I^{131}.

In Table V the results of treatment are shown in relation to the dose of I^{131} given. When a basic dose of seven millicuries was used, only one patient received a dose as low as five millicuries (all that was available at the moment), and a good result was obtained, though the calculated dose was seven millicuries. Of the remaining 31 patients in this group, 25 received either six or seven millicuries, and the results, which have been discussed in detail under Table III, were generally very good. Since 26 of the 32 with a basic dose of six millicuries received either five or six millicuries, 51 of the 64 patients received either the basic dose or one millicurie less. This number would have been even greater if occasionally another factor, such as age or gross exophthalmos, had not led to a reduction of the calculated dose.

TABLE V.

Results of Treatment of Diffuse Toxic Goitre with a Single Oral Dose of I^{131}.

Basic Dose of I^{131} (Millicuries.)	Results.	Dosage in Millicuries.						Total.
		4	5	6	7	8	9	
7	Excellent	—	1	12	10	2	1	26
	Hypothyroidism	—	—	1	1	—	—	2
	Persistent goitre with euthyroidism	—	—	—	1	2	1	4
6	Excellent	2	9	4	—	—	—	15
	Hypothyroidism	1	—	—	—	—	—	1
	Persistent goitre with:							
	(a) Euthyroidism	1	6	1	1	1	—	10
	(b) Hyperthyroidism	—	4	2	—	—	—	6
Total	Excellent	2	10	16	10	2	1	
	Unsatisfactory	2	10	4	3	3	1	

Two patients who received nine millicuries had retention figures of only 9% and 11%; in the one whose result ultimately was good, the calculated dose of 10 millicuries was reduced because she had apparently been hypothyroid formerly; over a year elapsed before the gland returned to normal size. Of the five who received eight millicuries, two had retention figures of 27% and 38·5% with the tracer test. Today, treatment of such patients with I^{131} would be postponed while efforts were made to increase the retention of iodine, the thyrotoxicosis if necessary being controlled meantime by antithyroid drugs. Of the other three patients who received eight millicuries, one had a retention figure of 48%, one retained 66·5% of the tracer dose, and the other was not subjected to a tracer test, but presumably the result would not have been low, since in only the last two of these five patients did the thyroid glands return to normal size.

Three of the 13 patients who received seven millicuries of I^{131} had unsatisfactory results. One is permanently hypothyroid and requires three grains of thyroid daily. Two have enlarged glands, but are euthyroid. One has a gland obviously enlarged, about four times the normal size, which gives no trouble. The retention of iodine in this goitre before treatment was only 55%. In the other patient the goitre was very large, and two millicuries were added to the basic dose of six millicuries for this reason; the retention in this gland was 83%. Goitres that are very large or that have a low retention of iodine need appreciably larger doses of I^{131}.

Four of the 20 patients receiving six millicuries of I^{131} had unsatisfactory results. One was mildly hypothyroid, one had an enlarged gland but was euthyroid, and in two hyperthyroidism persisted along with enlargement of the gland.

When the dose was less than six millicuries, satisfactory results were obtained in only half the cases. With a basic dose of seven millicuries results were very good. The much less satisfactory results with a basic dose of six millicuries were due to the decidedly smaller dose of I^{131} used. Of the 32 patients in this group, 23 received four or five millicuries, seven were given six millicuries, and one each received seven and eight millicuries respectively, the last-mentioned (discussed above) having a retention of only 27% of the tracer dose. The average dose of I^{131} in this group was 5·25 millicuries, while in the group with a basic dose of seven millicuries the average dose was 6·78 millicuries, an increase of nearly 30%.

From Table V it is obvious that a dose of six or seven millicuries of I^{131} is necessary to achieve a good result in the majority of patients with diffuse toxic goitre who have not been subjected to thyroid operation. The simplest method of treatment would be to give every such patient a dose of either six or seven millicuries of I^{131}. However, better results will be obtained by using a basic dose of seven millicuries, with appropriate modifications for the size of the gland and for results of tracer tests for retention of iodine by the thyroid. These tests are particularly valuable in discovering the small group of patients whose retention figures are unduly low (under 40% at twenty-four hours), but are not essential for the treatment of most patients with diffuse toxic goitre.

The use of a "basic" dose of seven millicuries of I^{131} with appropriate modifications means that most patients with diffuse toxic goitre will receive a dose of six or seven millicuries and should obtain a good result. The indications for a dose smaller than six millicuries in any such patient should be scrutinized most carefully, since a dose of this order should seldom be required. The dose should be greater than seven millicuries when the gland is very large. If the retention of iodine by the thyroid gland is decidedly low and attempts to increase the retention of iodine fail, the dose of I^{131} should be not less than nine millicuries.

Pregnancies following Treatment with I^{131}.

Six of the 18 married women aged under forty years who received I^{131}, the basic dose being seven millicuries, and who were followed for periods varying from eight months to two years, became pregnant. The three babies born up to date are healthy and the other pregnancies are proceeding normally. Of the 13 similar patients in the group with a basic dose of six millicuries, two became pregnant, though the follow-up period has been only from five months to one year.

Several patients became pregnant about three months after the I^{131} was given, practically as soon as they became euthyroid. This emphasizes the extreme importance of normal thyroid function with regard to fertility, a fact by no means generally recognized. This was stressed years ago by the senior author (Fairley, 1931), who reported the histories of two patients who were mildly hypothyroid after subtotal thyroidectomy for diffuse toxic goitre, and whose only complaint was sterility for four or more years after the operation. When given a small dose of thyroid, both became pregnant before their next menstrual period was due. About this time two other patients were examined with non-toxic goitres and complaints of sterility. On thyroid therapy one missed her next menstrual period and the other had one menstrual period before she also became pregnant. They received thyroid during the pregnancies and the babies were all normal at birth. The extreme rapidity of the action of thyroid in cases of sterility due solely to mild hypothyroidism has been confirmed in other cases since that time.

That larger doses of I^{131} may do little harm to the ovaries is shown by a case history recorded by Maloof *et alii* (1956). The patient, aged twenty-five years, had pulmonary metastases from a thyroid carcinoma, and over a period of a year received 140 millicuries of I^{131}. Subsequently she had two normal pregnancies, and the children, aged two and five years respectively, are well. There seems little risk of damage to the ovaries with a dose of about seven millicuries such as is used in diffuse toxic goitre.

The fœtal thyroid develops colloid about the fourteenth week of pregnancy, and thereafter may take up I^{131}. It is inadvisable, therefore, to use I^{131} later than the third month of pregnancy. Careful control with antithyroid drugs, the production of hypothyroidism being avoided, is usually the best treatment for diffuse toxic goitre during pregnancy. If necessary, I^{131} may be used after the birth of the child, though lactation is a contraindication to its use, because of the risk to the thyroid of the infant, since iodine is readily excreted in the milk. However, lactation is an extra strain that the thyrotoxic mother should rarely be asked to undertake.

The history of the only patient who was treated in this clinic during pregnancy is given below, though the case is not included in this analysis, since the patient was originally treated before the present system of dosage was introduced. The case illustrates also the undue prolongation of treatment with the use of very small doses of I^{131}.

Case 23.—Mrs. Q., aged twenty-five years, reported on January 5, 1951, with the history of having undergone subtotal thyroidectomy in April, 1944, for thyrotoxicosis, and a further operation in November, 1949, for a recurrent toxic goitre. In June, 1950, thyrotoxicosis recurred and was temporarily controlled by propylthiouracil, which resulted in hypothyroidism. After this was treated with thyroid, propylthiouracil failed to control the recurrent thyrotoxicosis. The right lobe of the thyroid was enlarged and apparently nodular; and the patient was restless, tremulous and sweating, with a pulse rate of 140 per minute. The protein-bound content was 9·2γ per 100 millilitres of serum. On March 9 she was given 3·5 millicuries of I^{131}, and on July 26 she received 1·5 millicuries. She remained mildly thyrotoxic, and on April 23, 1952, and again on November 13, 1952, she was given one millicurie of I^{131}, a total of seven millicuries over twenty months. On May 1, 1953, amenorrhœa had been present for two months, and she was nervous and tremulous, with a pulse rate of 120 per minute and a blood pressure of 150 millimetres of mercury, systolic, and 80 millimetres, diastolic. The protein-bound iodine content was 13·5γ per 100 millilitres of serum. The retention of a tracer dose of I^{131} at twenty-four hours was 79%. On May 21, 1953, about the eleventh week of her pregnancy, she was given a final dose of two millicuries of I^{131}. Subsequently she remained well. On November 6 the protein-bound iodine content was 7·2γ per 100 millilitres of serum (a good normal figure, since the protein-bound iodine content of the serum is usually increased by 2 to 3γ during pregnancy). On December 8 she was delivered of a healthy son weighing eight pounds, who has developed well. On August 2, 1954, she had a miscarriage at about three months, and in September, 1955, she had another healthy baby. When finally she was discharged from the clinic on December 16, 1955, she was in excellent health, and the thyroid gland was not palpable.

This patient would probably have been cured promptly by an initial dose of seven millicuries of I^{131}. Since the fœtal thyroid does not take up I^{131} until the fourteenth week of pregnancy, it was thought that a small dose of two millicuries of I^{131} at the eleventh week would not harm the fœtus, since twenty-four days after such a dose—that is, by the fourteenth week—not more than 0·25 millicurie of I^{131} would still be active in the tissues of the mother, and this amount would subsequently be reduced rapidly. Certainly no harm was done to the thyroid of the baby, and the mother was cured.

Post-Operative Recurrent Thyrotoxicosis.

Eleven patients with recurrent thyrotoxicosis presented at periods varying from eighteen months to thirty-one years after one or more operations on the thyroid gland, often in the interim having had courses of antithyroid drugs or iodine or both. Since little thyroid tissue is left after subtotal thyroidectomy, the goitre in such cases is usually small, and because of surgical distortion of the remnant of the gland, frequently appears to be nodular. But in the vast majority of cases the condition is a recurrence of what was primarily a diffuse toxic goitre, and the response to I^{131} therapy is correspondingly satisfactory.

In only one of these 11 patients was the goitre apparently a true nodular goitre.

A subtotal thyroidectomy had been performed thirty years previously when she was aged twenty-four years, and the goitre had reappeared fifteen years before she came under observation. The large goitre, with multiple nodules of varying consistency in both lobes and the isthmus, was associated with mitral stenosis and auricular fibrillation. A dose of eight millicuries of I^{131} was given on April 6, 1955, with subsequent reduction both in toxicity and in the size of the goitre. On November 30 another dose of eight millicuries of I^{131} was given, but the patient has not attended the clinic since.

Of the other 10 patients with recurrence of a diffuse toxic goitre, only one had a large goitre, and despite a dose of seven millicuries calculated from a basic dose of six millicuries, this gland remained unduly large, though the patient was euthyroid. In the other nine patients the goitre was smaller than that usually seen in cases of diffuse toxic goitre, and in only one was the gland even slightly larger than normal six months after I^{131} therapy; this patient was the only one to receive a dose of I^{131} as low as four millicuries.

Of the other eight patients, one was given eight millicuries, an addition of two millicuries being made because it was not then appreciated that the apparent nodularity of the gland was due to previous operation; the result was good. All four who received five millicuries obtained good results, though in one with auricular fibrillation present for the previous five years, this abnormal rhythm persisted despite apparent euthyroidism. Of three given six millicuries, one had no complaints, one was apparently euthyroid (protein-bound iodine content 4·3γ per 100 millilitres) but was subject to occasional short paroxysms of auricular fibrillation, and one, eleven months later, was taking one grain of thyroid daily to control mild hypothyroidism. This last patient was the only one in this group who (thirty-one years before, at the age of twenty-nine years) had been operated on for a non-toxic goitre.

Only in the one instance of true nodular goitre and in the one patient with an unusually large gland, whose history is given below, were the results unsatisfactory. In the other nine patients the gland returned to normal size, and eight became apparently euthyroid, while one was left with a mild degree of hypothyroidism.

Four of the seven patients on whom tracer tests were performed retained over 70% of the dose of I^{131} in the thyroid gland, the other three retaining 57%, 66% and 69% respectively. A higher proportion of these patients retained less than 70% of the tracer dose as compared with patients not previously subjected to operation for diffuse toxic goitre, but the numbers are too small to draw conclusions.

These satisfactory results of treatment with I^{131} in post-operative recurrent thyrotoxicosis justify the use of the same methods of estimating dosage as in cases of diffuse toxic goitre not treated surgically. Since in most patients the goitre is small, the use of a basic dose of seven millicuries will result usually in a dose of six millicuries, unless tracer tests reveal retention of 70% or more of the I^{131} given, when the dose would be five millicuries. Most of these patients therefore receive doses of five to six millicuries.

Any further recurrence is readily treated with I^{131}. Since previous operation distorts the anatomy of the region, risks to the recurrent laryngeal nerves and parathyroid glands are greatly increased at a second operation. The administration of I^{131} is the treatment of choice for recurrent thyrotoxicosis in patients previously operated on for diffuse toxic goitre.

The following histories are illustrative of this group of cases.

CASE 85.—Mrs. R., aged thirty-five years, was examined on November 20, 1954, with a history of operations on the thyroid gland in 1943 and 1945 for diffuse toxic goitre, and with classical symptoms of recurrent thyrotoxicosis present for a few months. The thyroid gland was not palpable, the pulse rate was 140 per minute and the blood pressure was 190 millimetres of mercury, systolic, and 90 millimetres, diastolic. The protein-bound iodine content was 11·0γ per 100 millilitres of serum and 71% of a tracer dose of I^{131} was retained in the thyroid gland at the end of twenty-four hours. On December 1 five millicuries of I^{131} were given. When she was discharged as cured on August 5, 1955, her weight had increased by more than a stone, the thyroid was not palpable, and she was euthyroid. Over the whole period only six visits were paid to the clinic, and if she had not been used in this investigation she would have been discharged earlier.

CASE 88.—Mr. S., aged fifty-three years, was referred by Dr. G. R. A. Syme on July 5, 1955, with a history of subtotal thyroidectomies, in 1936 for a very acute diffuse toxic goitre, and in 1946 for recurrent thyrotoxicosis associated with a large goitre. In 1949 a recurrence of thyrotoxicosis subsided after prolonged iodine therapy. Toxic effects followed the use of methylthiouracil. Since January, 1955, thyrotoxicosis had recurred, auricular fibrillation was present, the apex rate being 120 per minute, and exophthalmos was obvious. There was a gross diffuse enlargement of the thyroid gland, more pronounced on the right side, where the gland extended above the upper border of the thyroid cartilage. The retention of I^{131} at twenty-four hours was 73%. The protein-bound iodine content was 7·6γ per 100 millilitres of serum (a result of doubtful significance). On July 13 he received seven millicuries of I^{131} orally. By October 5 he had gained five pounds in weight and was working very hard. The gland was still large and hard. The apex rate was 72 per minute. He was taking "Digoxin" tablets, 0·5 milligramme daily. When he was last examined on February 20, 1956, he was well, had not been worried by the hot weather, and was still working strenuously. Auricular fibrillation persisted with an apex rate of 84 per minute, and there was little change in the thyroid gland, in the exophthalmos, or in his weight. The gland had decreased slightly while thyroid was given, but this had to be omitted because of nervous symptoms.

Though the patient is satisfied with this considerable improvement, it is not a good result, since the gland is still large. When he was treated, six millicuries was the basic dose. With the history of repeated recurrences and the large size of the goitre, a dose of nine millicuries would have given a better result. All other patients in this group needed only a single dose of I^{131} for their cure.

TOXIC NODULAR GOITRE.

Operation is the treatment of choice for toxic nodular goitre. If operation is contraindicated, thyrotoxicosis can be controlled by I^{131}, but the nodules will often persist, although considerably reduced in size.

The initial dose of I^{131} in the 17 cases in this group was estimated in the same way as for cases of diffuse toxic goitre, and proved to be much too low. Toxic nodular goitres require from two to three times the dose used for diffuse goitres, perhaps because of the variable uptake of I^{131} in different parts of the nodular gland. Unlike diffuse toxic goitres, the risk of subsequent hypothyroidism is negligible in these cases. McCullagh (1952) states that myxœdema has never been observed in patients with toxic nodular goitre after treatment with I^{131}. Since the majority of these patients are also aged over fifty years, larger doses of I^{131} than are used in diffuse toxic goitre may be given without undue worry regarding either hypothyroidism or the remote possibility of any carcinomatous change many years later.

All patients in this group who were given initial doses of I^{131} up to eight millicuries and were followed for a year or more relapsed, and have been or will be given another dose. Eight received two doses totalling from 16 to 20 millicuries, and one had three doses totalling 24 millicuries. To date none of those followed for more than a year after the last dose has relapsed.

All seven patients with auricular fibrillation were treated with "Neo-mercazole" after I^{131} had been given. Three reverted to normal rhythm, one in three weeks (obviously owing to the drug and not the I^{131}), one between three and ten weeks, and one between six and ten weeks after I^{131} therapy. Two of the four with persistent fibrillation also had mitral stenosis. Quinidine might have been of value in the treatment of the other two, but has not been used.

In estimating the dose of I^{131} for patients with toxic nodular goitre, the essential factor is the knowledge that the condition is a true nodular goitre. A dose of about 15 millicuries of I^{131} should be given in every case. If the gland is very large, or if the retention of I^{131} by the

goitre is below 60% twenty-four hours after a tracer dose, an appropriate increase in the dose should be made.

A detailed analysis of these cases is unnecessary, but the following two histories illustrate some of the problems in treatment.

CASE 47.—Mrs. T., aged sixty-eight years, was referred by Dr. B. Hudson on July 2, 1954, with a history of *diabetes mellitus* of one year's duration and of thyrotoxicosis of two months' duration. The weight, formerly 182 pounds, was 120 pounds. A small, firm, nodular thyroid gland extended slightly retrosternally on the right side. The protein-bound iodine content was 10·2γ per 100 millilitres of serum. "Neo-mercazole" was prescribed, and on July 28 five millicuries of I^{131} were given. "Neo-mercazole" administration, omitted for three days before the I^{131} was taken, was resumed from July 31 until September 24, 1954. On October 24 the patient's weight had increased by one stone, she could do her housework and the thyroid gland was not palpable. On March 4, 1955, her condition was unchanged. When she was next examined on July 15, 1955, palpitation and dyspnœa, even at rest, had been troublesome for six weeks. The thyroid gland was slightly enlarged, and auricular fibrillation and congestive cardiac failure were present, the heart rate being 144 per minute. The protein-bound iodine content was 10·2γ per 100 millilitres of serum. On July 27 12 millicuries of I^{131} were given, and on August 1 the administration of "Neo-mercazole", 30 milligrammes per day, and of Lugol's solution of iodine, 30 minims per day, was commenced. There was no response to this treatment, and though the diabetes was well controlled, death occurred on August 6, 1955. At autopsy the thyroid gland was enlarged and nodular.

The second dose of I^{131} had no time to exert any effect, but since there was no benefit from Lugol's solution of iodine, operation at this stage was out of the question. The original dose of five millicuries of I^{131} could well have been trebled and the ultimate result might have been better. At that time, a year before her death, operation would probably have been successful. This is the only death due to thyrotoxicosis in the series. Another patient cured of thyrotoxicosis died from carcinoma of the bronchus and pulmonary tuberculosis.

CASE 33.—Mrs. U., aged sixty-eight years, was referred by Dr. R. Kerr on June 27, 1954, with a history of congestive cardiac failure not responding to routine treatment. A goitre had been present for at least thirty years. For fifteen years there had been increasing dyspnœa, palpitation and weakness, more severe over the past year, during which 28 pounds in weight had been lost. The thyroid gland was moderately enlarged, with one large, almost circular nodule, 3·5 centimetres in diameter, in the isthmus. Gross congestive cardiac failure with auricular fibrillation (rate 126 per minute) was present. The protein-bound content was 14·0γ per 100 millilitres of serum. On May 21 seven millicuries of I^{131} were given intravenously, since persistent vomiting prevented oral administration. This was the only instance in which the oral route was not used. Three days later "Neo-mercazole", 15 milligrammes per day, was given, and on June 10 the heart reverted to normal rhythm. "Neo-mercazole" was not omitted until September 3, when she felt "marvellously better" and the thyroid was smaller and softer, as was the central nodule. On December 3 she could do some light housework, although digitalis was necessary along with an injection of a mercurial diuretic every ten days to control œdema. On March 18, 1955, the cardiac rhythm was normal, but there was some dyspnœa on mild exertion. On June 14 she had pain across the front of the chest, and this persisted until June 17, when auricular fibrillation was found to have recurred. The thyroid nodule was about one-third of its original size. The hands were cool and dry, and there was slight pitting œdema about the ankles. The clinical findings were unchanged when, on October 28, she reported that an episode of mild congestive cardiac failure a few weeks previously had kept her in bed for a week. On November 16 the protein-bound iodine content was 6·5γ per 100 millilitres, a normal result; but the persistence of the auricular fibrillation suggests that another dose of I^{131} is indicated. This would be useful whether there is recurrent hyperthyroidism or not.[1]

[1] This patient was next examined in hospital on October 2, 1956, when there was a history of a recent slight increase in the size of the goitre. Auricular fibrillation and congestive cardiac failure were present. Death occurred suddenly three days later, and autopsy revealed a moderately enlarged nodular goitre, with extensive thrombosis in both branches of the pulmonary artery, commencing one centimetre below its bifurcation, extending widely through the smaller arteries, and in the lower lobes reaching almost to the periphery of the lungs.

The use of I^{131} to reduce the metabolic rate in patients with congestive heart failure or *angina pectoris* when there is no question of hyperthyroidism has proved of value in very many reported cases, and in a limited experience it has been found useful in this clinic.

DISCUSSION.

In the treatment with I^{131} of patients with diffuse toxic goitre the chief difficulty is the estimation of the requisite dose. Of the three factors used to modify the basic dose of seven millicuries in this series, the size of the goitre is most important. The greatest value of the tracer test is in revealing the small group of patients whose retention of iodine by the thyroid gland is unduly low.

The modification of dosage for thyrotoxicosis of less than average severity has been abandoned for reasons already given. For hyperthyroidism of greater than average severity most observers increase the dose of I^{131}, though in this series it was decreased in the relatively few cases of very severe hyperthyroidism. Most of such patients have a retention of at least 70% of iodine by the goitre at the end of twenty-four hours, and when such tests are available the dose is reduced by one millicurie for this high retention, the calculated dose being six millicuries. Since doses of less than six millicuries of I^{131} are not likely to achieve a complete cure, and since there is a difference of opinion about increasing or decreasing the dose for this factor, it has also been discarded in the estimation of the requisite dose.

A further series of patients is now being treated, in which the basic dose of seven millicuries is altered only for the size of the gland and, if tracer tests are performed, for the degree of retention of iodine by the goitre; the adjustments for the latter results have been detailed above. This simpler method of estimating the required dose of I^{131} should prove equally satisfactory.

Another problem in the use of I^{131} is the suggested risk of supervention of carcinoma of the thyroid gland twenty or more years after treatment. For this reason some workers limit its use to patients aged over forty years. This risk appears negligible for adults and has been discussed fully by Blomfield *et alii* (1955). Some evidence suggests that, in infants, irradiation of the thymus gland may later be followed by an increased incidence of carcinoma of the thyroid gland (Duffy and Fitzgerald, 1950; Simpson *et alii*, 1955; Clark, 1955). Apparently infants react differently from adults. No case of carcinoma of the thyroid gland has been reported from the use of radio-iodine in the sixteen years since its introduction, although many patients have received much higher doses than are used in thyrotoxicosis.

With the dosage of I^{131} used in hyperthyroidism it seems utterly improbable that mutation effects from damage to the genes will occur, though an authoritative answer to this problem can hardly be given until a century or more has passed. The radiation received by the ovaries after an oral dose of 10 millicuries of I^{131} has been estimated as about the same as they receive with a routine X-ray pelvimetric examination.

Most of the radioactivity of I^{131} is due to β rays, which travel about two millimetres in body tissues; hence structures such as the parathyroid glands close to the thyroid are not damaged by these rays. With a half-life of eight days, about 93% of a dose of I^{131} is dissipated in a month, and about 99·5% in two months, so damage from excessive dosage is limited. The relatively small therapeutic doses used for toxic goitres do not damage the urinary apparatus or affect menstruation.

SUMMARY AND CONCLUSIONS.

1. Operation is the treatment of choice for toxic nodular goitres, though if operation is contraindicated, toxicity can be controlled by I^{131} therapy, the dose necessary being two to three times as great as that required in diffuse toxic goitres. A suitable initial dose in such cases is 15 millicuries of I^{131}.

2. In the treatment of diffuse toxic goitre the administration of I^{131} has many advantages over operation, and

certainly is the treatment of choice for post-operative recurrent diffuse toxic goitre. The chief difficulty in treatment is the estimation of the requisite dose.

3. Usually treatment involves swallowing a single dose of I^{131}, the full effect of which is not manifest in less than three months. There is an absence of mortality and no risk of vocal cord paralysis or tetany with this ambulatory treatment.

4. A simple, satisfactory method of estimating the required dose of I^{131} is to use a basic dose of seven millicuries and to modify this according to the size of the thyroid gland and the retention of iodine by the goitre, when this is known. Though in this series adjustment of the dose was also made for the degree of thyrotoxicosis, this factor has now been discarded.

5. Most patients with diffuse toxic goitre can be treated satisfactorily without knowledge of the retention of iodine by the goitre, as estimated by a tracer test, which, however, is of great value in revealing the occasional patient with an unusually low retention of iodine. This frequently is due to the ingestion of iodine, therapeutically or otherwise, in the preceding few weeks. In patients with a very low retention of iodine, I^{131} therapy should be postponed for some weeks while efforts are made to increase this retention.

6. Alteration of the dose of I^{131} for other factors, such as youth or gross exophthalmos, proved unsatisfactory.

7. The excessive or prolonged use of antithyroid drugs after I^{131} therapy often results in temporary hypothyroidism and an increase in the size of the goitre, which may take many months to subside. The drugs should be omitted for at least twenty-eight hours before and for forty-eight hours after I^{131} is given. Thereafter they should rarely be used for longer than six weeks, by which time the I^{131} is being effective.

8. It is always preferable to deal with patients who have received no previous treatment for their hyperthyroidism. Unsatisfactory results are usually due to prior therapy with iodine or to unduly prolonged or excessive dosage with antithyroid drugs.

9. When rapid control of the hyperthyroidism is indicated, operation may be preferable to administration of I^{131}.

10. The only contraindications to the use of I^{131} are pregnancy (except perhaps in the first ten weeks) and lactation, because of the risk to the thyroid of the infant, though the thyrotoxic mother should seldom be subjected to the added strain of lactation.

11. A dose of six or seven millicuries of I^{131} usually gives satisfactory results in diffuse toxic goitre. The indications for doses higher or lower than these amounts should be carefully scrutinized, though for unknown reasons overseas observers have found the satisfactory range of dosage generally to be from six to twelve millicuries.

12. Since most patients with post-operative recurrent diffuse toxic goitre have small goitres, the dose of I^{131} in these cases is usually five or six millicuries.

13. An appreciable rise in the diastolic blood pressure is sometimes one of the earliest signs indicating the development of hypothyroidism after I^{131} therapy.

14. The common occurrence of pregnancy soon after these patients become euthyroid emphasizes the importance of normal function of the thyroid gland in fertility.

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EPIDEMIOLOGY OF TETANUS IN QUEENSLAND.

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REPORTS on the epidemiology of tetanus in Australia have been few. Langton-Lockton (1951) reviewed the incidence of the disease in Victoria over the period from 1931 to 1950, and observations on some aspects of tetanus in South Australia have been recorded by Beare (1953). Yet tetanus remains an important infectious disease. For the four years from 1950 to 1953 tetanus was responsible for 30% of all deaths in Australia from typhoid, paratyphoid, bacillary dysentery, scarlet fever, diphtheria, whooping-cough, tetanus, measles, mumps and smallpox combined. Tetanus, moreover, is a completely preventible disease.

Of particular interest was the fact that of 663 deaths from tetanus in Australia for the decade 1944 to 1953 no fewer than 192 occurred in Queensland. This is double the number expected on a population basis (see Figure I), and it therefore seemed appropriate to review the case histories of tetanus patients admitted to the Brisbane General Hospital and to the Brisbane Children's Hospital to ascertain whether any factor operated in Queensland to cause such a disproportionate number of deaths. Accordingly, I have analysed the case records of more than 200 patients admitted with a clinical diagnosis of tetanus to the above-mentioned institutions for the years 1943 to 1955. When cases in which the diagnosis was doubtful were excluded (such as hysteria, inflammatory conditions of the mouth, meningeal inflammation *et cetera*), there remained 190 cases in which the diagnosis of tetanus was reasonably satisfactory. Analysis of these cases comprises the present report.

Geographical Distribution.

All the patients, with the exception of a few referred from smaller hospitals near Brisbane, resided in the Greater Brisbane area. This comprises 375 square miles and includes some districts devoted to dairying and to small-crop farming.

Comparison with Notified Cases of Tetanus.

For the seven years from 1948 to 1954 tetanus notifications in Queensland have totalled 215, and it is of

interest to compare the age and sex distributions of these notified cases with those of the present series. As shown in Table I, the two series are comparable as far as age and sex are concerned.

Age Distribution of Cases.

The age distribution of the of the 190 patients is shown in Table II and Figure II. No fewer than 90 patients (47·4% of the total) were under the age of fifteen years, whereas this age group comprised only 27·8% of the population of Queensland (1947 census). There is thus a highly significant number of patients in this particular age group, and it is clear that the risk of tetanus is highest in children. Apart from cases of neonatal tetanus, no patient was younger than two years of age. The oldest patient was aged eighty-eight years. Of the children, 25 were aged under five years and 37 were in the five to nine years age group.

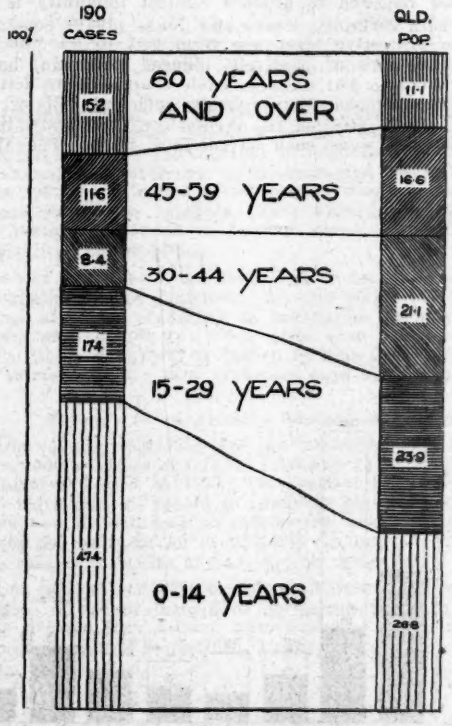

FIGURE I.

Showing percentage age composition of 190 cases and population of Queensland (1947 Census).

Occupations of Patients.

The occupations followed by the patients are listed in Table III. Farmers and farm workers provided ten cases. This is a high incidence, for farming is not a major industry in the Greater Brisbane area. Eight patients were pensioners. Pensioners frequently sustain accidents around the house. They have lost much of their former strength and dexterity and they tend to neglect injuries. Of the female patients, 23 were children.

Probable Portal of Entry.

In 144 cases it was possible to determine with reasonable accuracy the probable injury that afforded entry to *Clostridium tetani*. In 56 cases, on the other hand, the portal of entry could not be determined, either because there was no obvious external sign of injury or because more than one lesion was sustained on different occasions.

The probable portal of entry for tetanus spores is set out in Table IV, together with the number of deaths associated with the particular lesion listed.

Punctured Wounds.

Punctured wounds (for example, by nail, stick, splinter, bone *et cetera*) comprised 75 cases (52%), and were responsible for more than half of the deaths. Of these wounds, 65 were in the feet. Punctured wounds were rather less frequent in females than in males. Punctured wounds of the feet were responsible for the following percentages of wounds of entry in these male age groups: under twenty years, 38%; twenty to thirty-nine years, 24%; forty to fifty-nine years, 21%; over sixty years, 21%. In other words, these injuries are most frequent in childhood and in adolescence.

Lacerations.

Lacerations of various types were the probable portal of entry in 20 males and in six females, representing 18% of the cases.

Surgical Operation, Abortion and Childbirth.

Ten patients (three males and seven females) developed tetanus from surgical operations, abortions or childbirth. The following operations contributed one case each: vaginal hysterectomy, hæmorrhoidectomy, repair of cystocele, colporrhaphy and ventrosuspension, dental extraction, radical cure of hydrocele and removal of tonsils and adenoids. Tetanus bacilli were grown from dust on the floor of the operating theatre where one patient underwent an operation, and in another instance were grown from the powder used with the rubber gloves. Two patients developed tetanus a few days after normal childbirth with only minor tissue damage. In two cases of septic abortion tetanus developed. In one of these, tetanus bacilli were grown in cultures made from areas of pulmonary infarction (Tonge, 1947); this indicates that *Cl. tetani* may on occasion travel far from its site of entry.

Neonatal Tetanus.

Seven infants had neonatal tetanus. In one case tetanus bacilli were grown from umbilical pads similar to those applied to the infant. These pads had been imperfectly sterilized and had then been stored in methylated spirit.

Planned Aseptic Procedures.

With the exclusion of the two cases in which tetanus followed septic abortion, 15 patients (8%) developed tetanus after planned aseptic procedures (such as operation and confinement) carried out in hospitals. The occurrence of several cases from these causes provoked an extensive review of sterilization methods commonly used in Queensland hospitals. It was found that many of these were faulty, and that autoclaves operating at 15 pounds pressure of steam had such a narrow margin of safety that they had to be regarded as potentially unsafe. A booklet setting out recommended techniques for sterilizing various items was issued to all hospitals in 1953, and since then I am not aware of any instance in which tetanus has been contracted in a hospital.

Miscellaneous Injuries.

Miscellaneous injuries included infected toe nail (two cases), varicose ulcer, paronychia, compound fracture of the forearm, laceration of the tongue, dog bite, and penicillin injection for *otitis media*. In the last-mentioned the syringe had been "sterilized" by immersion in methylated spirit; but tetanus has frequently been reported in cases of discharging *otitis media*.

Incubation Period.

Owing to the tendency of the organism to lie latent in wounds, reported incubation periods have been variable. Rosenau and Anderson (1943) showed that the incubation period was directly proportionate to the amount of toxin formed. Guinea-pigs given large doses of toxin developed symptoms on the third day, and as the dose of toxin decreased symptoms took longer to develop.

TABLE I.

Showing Age and Sex Distribution of 190 Hospital Cases and of 215 Notified Cases of Tetanus in Queensland.

Age Group. (Years.)	Hospital Cases.[1]				Notified Cases.[2]			
	Male Patients.	Female Patients.	Persons.	Percentage of Total.	Male Patients.	Female Patients.	Persons.	Percentage of Total.
0 to 14	68	22	90	47·4	101	35	136	52·5
15 to 29	27	6	33	17·4	36	9	45	17·4
30 and over	44	23	67	35·2	57	21	78	30·1
All ages ..	139	51	190	100·0	194	65	259	100·0

[1] Male-female ratio, 2·7. [2] Male-female ratio, 3·0.

Boyd (1946) reported the incubation periods in 57 unimmunized servicemen during World War II as being between ten and twenty-one days. Of Boyd's patients 10% had incubation periods of less than seven days and 21% had incubation periods of between seven and ten days. Another series of 58 patients had a mean incubation period of 8·4 days, with 29% less than seven days and 39% between seven and ten days (Diaz-Rivera, Deliz and Berio-Saurez, 1948). Sachs (1952) quotes a peak incubation period of eleven to twelve days. In the present series the approximate incubation periods could be estimated in 129 cases, and details are provided in Table V and Figure III. Thirty patients (26%) had incubation periods of less than seven days, 49 (38%) between seven and ten days, and 30 (23%) between ten and fourteen days. The incubation periods ranged from three to thirty-four days, with a mean of 9·1 days.

TABLE II.

Showing Age Distributions of 190 Cases of Tetanus.

Age Group. (Years.)	Males.	Females.	Persons.	Percentage of Total.	Expected Number.[1]
0 to 14 ..	68	22	90	47·4	51
15 to 29 ..	27	6	33	17·4	45
30 to 44 ..	11	5	16	8·4	41
45 to 59 ..	16	6	22	11·6	32
60 and over ..	17	12	29	15·2	21
All ages ..	139	51	190	100·0	190

[1] If the number of cases occurring was in proportion to the age distribution of the population of Queensland (1947 census).

Examples of short incubation periods (three days) were as follows:

A man, aged seventy years, ran a splinter into his right forearm on March 16, 1953. On the evening of March 18 he developed trismus and a rigid right arm. After a typical course, during which his right arm remained rigid throughout, he died on March 25.

A boy, aged five years, cut his left great toe on November 5, 1951. On the evening of November 7 he woke up complaining that he could not open his mouth. He also had some body twitching. He died on November 10.

Prophylaxis with Tetanus Antiserum.

There is a record of administration of tetanus antiserum prophylactically in only 12 cases (7%). Apparently the average person disregards the minor injuries that are responsible for most cases of tetanus and does not seek medical attention until symptoms of the disease develop. In view of this attitude, it is obvious that tetanus antiserum cannot be expected to reduce significantly the incidence of tetanus in a community. Only widespread active immunization will do that.

Some details of the 12 patients who received antiserum prophylactically are given in Table VI. Four of these patients received 500 units, a grossly inadequate dose even for a child. While the actual level of antitoxin in the blood required to produce clinical immunity is not known with certainty, Cooke and Jones (1941) concluded that the protective level was from 0·01 to 0·1 unit per cubic centimetre of passively induced antitoxin, but a level of 0·001 to 0·01 unit per cubic centimetre in actively immunized persons was probably sufficient. Bigler and Werner (1941) titrated the serum antitoxin levels in 64 children who were each given 1500 units. The titres varied widely, but during the third week the tendency was for the levels to fall to 0·01 unit per cubic centimetre, though some had levels as high as 0·1 unit and others fell below 0·003 unit. Thus the minimum protective dose for a child is about 1500 units. Adults would require a minimum dose of 3000 units. In view of the rapid fall of antitoxin levels in the blood following the intramuscular injection of doses of 1500 to 3000 units, complete protection in an unimmunized subject can be assured only if the dose is repeated at the end of a week or ten days, because tetanus antitoxin has a definite effect in prolonging the incubation period. In the 12 patients who received antiserum the mean incubation period was thirteen days.

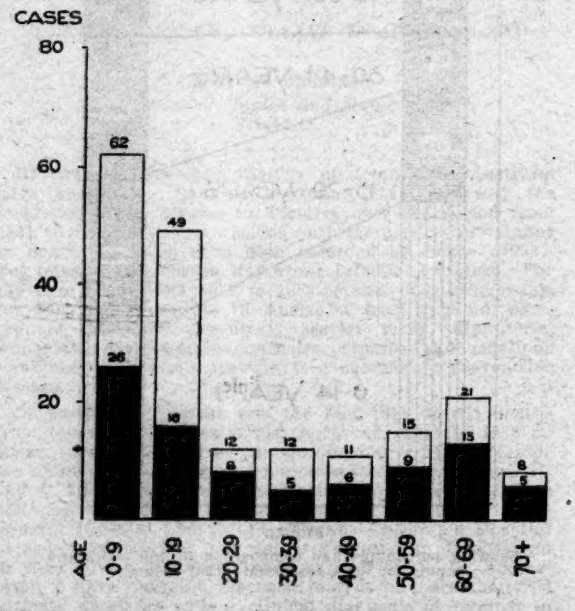

FIGURE II.

Tetanus in Queensland. Age distribution of 190 cases and 89 deaths (shaded columns).

TABLE III.

Showing Status or Occupation of 139 Male and 51 Female Patients with Tetanus, of Whom 89 Died.

Males.			Females.		
Status or Occupation.	Patients.	Deaths.	Status or Occupation.	Patients.	Deaths.
New-born infant	3	1	New-born infant	4	3
Pre-school child	11	4	Pre-school child	7	5
School child	56	22	School child	12	2
Farmer	10	5	Domestic duties	19	10
Pensioner	8	6	Pensioner	2	—
Transport worker	6	4	Miscellaneous	4	2
Engineer	5	3	Unknown or unstated	3	—
Labourer	4	2			
Clerk	3	—			
Cook	2	1			
Seaman	2	1			
Gardener	2	—			
Retired	2	2			
Miscellaneous	11	8			
Unknown or unstated	14	8			
Total	139	67	Total	51	22

Deaths.

Deaths totalled 89, or 47% of all cases. Tetanus still carries the highest mortality of any common infectious disease, and the introduction of modern treatment (for example, relaxant drugs, tracheotomy and wound excision) has not been attended so far by any dramatic fall in the death rate. For example, there were 15 deaths among 34 patients admitted to hospital since January, 1953—a mortality rate of 44%.

As is well known, the death rate in tetanus falls as the incubation period increases. In this series the mortality rates arranged according to incubation periods for 129 cases were as follows: 100% (less than five days); 81% (five to six days); 61% (seven to nine days); 30% (ten to thirteen days); 19% (fourteen days and over).

Tetanus in an Actively Immunized Subject.

One of the patients was an ex-serviceman who had received two doses of tetanus toxoid in 1940. He developed tetanus and died in 1952. This patient had not received the third dose of toxoid to complete his basic immunization, and he had had no reinforcing doses. Although he could not be regarded as properly immunized, such cases are rare in civil life and are worth recording.

One patient sustained a punctured wound and was given a dose of toxoid instead of antiserum when the wound was dressed. No matter how laudable the motive, this procedure cannot be justified, because a first dose of tetanus toxoid will not produce demonstrable antibodies for about two months.

Death Rate and Prophylaxis with Antiserum.

Of 12 patients who were given tetanus antiserum within twenty-four hours of injury, three died. Although the number of cases is small, this tends to confirm previous reports that the prophylactic administration of antiserum increases the chance of survival in those who subsequently develop tetanus.

Death Rate According to Age and Sex.

Deaths according to sex and to fifteen year age grouping are set out in Table VII. The death rate for females was about 5% lower than that for males, but was 10% higher than for males in the nought to fourteen years age group. In general the death rate increased with age, and in patients aged over sixty years it attained 65%.

Discussion.

As was indicated earlier, my chief motive in undertaking analysis of these cases was to endeavour to find the reason why Queensland, with 15% of the population, contributed 34% of all deaths from tetanus in Australia during the decade 1944 to 1953. This can be expressed in another way. The number of deaths from tetanus in Australia in 1953 was 71, but if the mean death rate from tetanus in Queensland for the decade 1944 to 1953 was

TABLE IV.

Showing Probable Portal of Entry for Clostridium Tetani in 144 Cases of Tetanus, 75 Fatal.

Type of Injury.	Cases.				Deaths.			
	Male Patients.	Female Patients.	Persons.	Percentage of Total.	Male Patients.	Female Patients.	Persons.	Percentage of Total.
Punctured wound:								
Upper limb	7	3	10	6·9	4	2	6	8·0
Lower limb	49	16	65	45·1	29	7	36	48·0
Laceration:								
Upper limb	4	1	5	3·5	3	—	3	4·0
Lower limb	13	4	17	11·8	5	2	7	9·3
Elsewhere	3	1	4	2·8	1	1	2	2·7
Surgical operation, confinement or abortion	3	7	10	6·9	1	5	6	8·0
Neonatal tetanus	4	3	7	4·9	1	3	4	5·3
Contusion, bruise	8	1	9	6·3	3	—	3	4·0
Abrasion	3	2	5	3·5	2	1	3	4·0
Multiple injuries	2	1	3	2·1	1	—	1	1·4
Miscellaneous lesions	6	3	9	6·2	4	—	4	5·3
Total	102	42	144	100·0	54	21	75	100·0

applied to Australia the number of deaths in 1953 would have been 148. This is a highly significant difference and only two explanations are possible.

The first explanation is that the death rate in Queensland is much higher than in the other States. If this was so it could be due either to shorter incubation periods in Queensland cases or to less effective methods of treatment. The mean incubation period of the cases reported here does not differ significantly from mean incubation periods reported elsewhere. This possibility can therefore be disregarded. The death rate in this series was 47%, whereas the death rate in the South Australian cases reported by Beare was 31%. This difference would be significant only if the age and sex distribution of the two series was identical (which it was not), and if the criteria for diagnosis were the same in each series. In the discussion which followed the presentation of Beare's paper it was revealed that the death rate of tetanus at the Adelaide Children's Hospital was 39%, whereas in my series there were 26 deaths among 62 children aged under ten years, this being approximately the same rate. It is thus unlikely that the death rate is significantly higher in Queensland than in other States.

TABLE V.

Showing Estimated Incubation Periods in 129 Cases of Tetanus.[1]

Days.	Male Patients.	Female Patients.	Persons.	Percentage of Total.
0 to 4 ..	2	2	4	3·1
5 to 6 ..	23	7	30	23·3
7 to 9 ..	37	12	49	38·0
10 to 13 ..	22	8	30	23·3
14 to 20 ..	11	3	14	10·8
21 and over ..	1	1	2	1·5
Total	96	33	129	100·0

[1] Range, 3 to 34 days; mean, 9·1 days; standard deviation, ±4·1.

The other possible explanation is that the incidence of the disease is much higher in Queensland than in the rest of Australia. The evidence in favour of or against this hypothesis is unsatisfactory. Some States do not require notification of tetanus, while in others it has been notifiable for such a short period that the figures are still unreliable. It will require several years of notification in other Australian States before the relative incidence in various parts of Australia can be determined. It is, however, a reasonable assumption that the incidence is higher in Queensland. Factors that may operate in this State include the relatively large proportion of the population (62% in 1954) residing outside the capital city as compared with other States, and the favourable climate which enables children to go without footwear throughout the year. Indeed, it is surprising to note the large number of men in Brisbane who work barefoot around their homes at week-ends.

Another feature emerging from this analysis is the high incidence of tetanus in children. They provided 47% of all the cases reported here. Children frequently sustain injuries which favour the growth of tetanus bacilli, and active immunization is clearly desirable. It is pleasant to record that 38% of children attending school in Queensland for the first time in 1955 had received basic immunization against tetanus, and recent introduction of triple antigen must rapidly increase this figure. When most children in this State have been properly immunized against tetanus there should be a substantial decline in the number of notified cases.

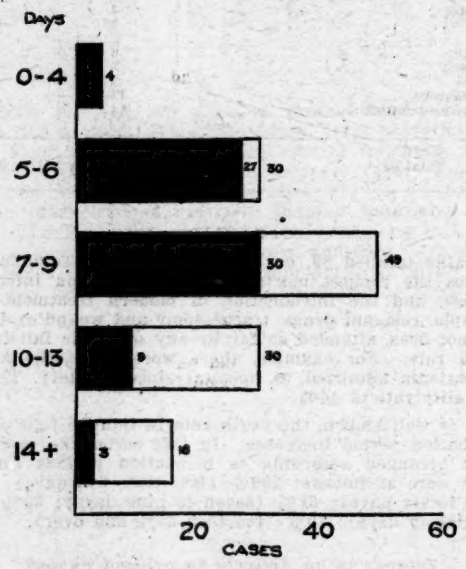

FIGURE III.

Showing incubation periods of 129 cases of tetanus, of which 73 cases (shaded portions) were fatal.

Worthy of mention also is the occurrence of 15 cases (8%) of tetanus following planned aseptic procedures such as confinement and surgical operation. Greater care in sterilization procedures in hospitals has led to the disappearance of cases from this source over the last three years.

Summary.

Of the deaths from tetanus in Australia over a ten-year period from 1944 to 1953, Queensland had more than twice the number expected on a population basis.

To ascertain the reasons for this, the case records of 190 tetanus patients admitted to Brisbane public hospitals

TABLE VI.

Showing Details of 12 Tetanus Patients Who Received Tetanus Antiserum Prophylactically within Forty-eight Hours of Injury.

Year.	Sex.	Age. (Years.)	Dose. (International Units.)	Days Since Injury.	Injury.	Incubation Period. (Days.)[1]	Severity of Disease.
1948	M.	6	500	0	Compound fracture of the hallux.	18	Mild.
1953	M.	8	500	0	Trod on nail.	12	Fatal.
1944	M.	14	500	0	Laceration of leg.	34	Mild.
1950	M.	61	500	0	Trod on nail.	10	Fatal.
1945	M.	20	1500	0	Gross laceration of the ankle.	15	Severe.
1950	M.	50	1500	0	Trod on nail.	11	Mild.
1953	M.	62	1500	0	Laceration of the foot.	10	Moderate.
1949	F.	4	Unknown.	0	Laceration of the foot.	17	Fatal.
1954	M.	88	Unknown.	0	Laceration of the knee.	7	Moderate.
1950	M.	9	Unknown.	1	Trod on nail.	8	Fatal.
1949	M.	41	Unknown.	0	Laceration of the foot.	11	Mild.
1952	M.	58	Unknown.	0	Multiple injuries.	5	Fatal.

[1] Mean incubation period, 13·2 days (standard deviation, 7·2).

TABLE VII.

Showing Number of Deaths and Death Rate in 190 Cases of Tetanus, According to Age.

Age Group. (Years.)	Patients.			Deaths.			Percentage of Deaths.		
	Males.	Females.	Persons.	Males.	Females.	Persons.	Males.	Females.	Persons.
0 to 14	68	22	90	24	10	34	35·3	45·5	37·8
15 to 29	27	6	33	13	3	16	48·1	50·0	48·5
30 to 44	11	5	16	5	1	6	45·5	20·0	37·5
45 to 59	16	6	22	11	3	14	68·8	50·0	63·6
60 and over ..	17	12	29	14	5	19	82·4	41·7	65·5
All ages ..	139	51	190	67	22	89	48·2	43·1	46·8

have been analysed. In age and sex distribution these cases were comparable with notified cases of tetanus.

Children aged under fifteen years provided 90 cases (47%), whereas this age group represented only 28% of the Queensland population. The high incidence in children is significant.

The probable portal of entry of infection was ascertained in 144 cases. Punctured wounds comprised 75 (52%) of these, and 65 punctured wounds were on the feet. Lacerations caused 28 cases (18%), and surgical procedures (operation, confinement, abortion) caused 17 cases (12%).

In 129 cases the mean incubation period was 9·1 days, which is similar to incubation periods reported elsewhere.

Only 12 patients (7%) had received antiserum prophylactically. While so few attend for medical treatment of wounds that could result in tetanus, antiserum can play only a minor role in prevention. Widespread active immunization is the only way to reduce the incidence of tetanus. When tetanus antiserum was given for prophylaxis the dose was usually inadequate.

The over-all death rate was 47%. The death rate varied according to the incubation period, being 100% for incubation periods of less than five days and 19% when the incubation period exceeded two weeks. The death rate increased with the age of the patient.

The only conclusion possible is that there are more deaths in Queensland because there are more cases. The relatively high incidence is probably due to the high proportion (62%) of the population living outside the capital city and to the favourable climate which permits children to go barefoot throughout the year.

Acknowledgements.

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RECENT ADVANCES IN THE STUDY OF SUBFERTILITY.[1]

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SIR WILLIAM OSLER (1903) once wrote that "we doctors do not take stock often enough, and are apt to carry on our shelves stale, out-of-date goods". This paper attempts both to pick a pathway through the maze of new ideas which have appeared in the published literature, especially during the last five years, and to select those ideas which offer a reasonable chance of being called a recent advance. This will at least serve as a stimulus to us all, because we tend to see only what we look for and to look for only what we know.

I should like to start with a basic truth which every recent advance has attested to be true. This is the fact that the causes of subfertility in most patients can be found neither by an inspection of the pelvic organs with the unaided and naked eye, nor by a simple pelvic examination. They can be found only with the assistance of the microscope, the thermometer, X rays, carbon dioxide gas and the culdoscope (Decker, 1952).

Problems in infertility are at the present day one of the most fruitful fields for new research work; I submit that we in Australia are not playing our part. We tend to believe in the theory of diagnostic and therapeutic nihilism which has been preached by a few authors (Snaith *et alii*, 1953; Stallworthy, 1948; Bender, 1952; Jeffcoate, 1954; Buxton, 1955) and to let others overseas do our thinking. We should have our own Australian society for the study of fertility to promote more original investigation and research, and it should include veterinarians, biochemists and allied scientists.

RECENT ADVANCES IN THE STUDY OF SUBFERTILITY IN THE MALE.

As gynæcologists we are called upon to advise our patients about the forms of investigation and treatment available for their husbands. This is my excuse for noting a few new ideas in this field.

Revised Criteria of a Normal Sperm Count.

The first recent advance is a new conception of what constitutes a normal sperm count. In the past our standards of normal counts have been too high and have over-emphasized morphological as opposed to physiological aspects.

In 1950 I investigated the sperm counts of 263 fathers (Grant, 1951) and found that according to the current standards only 44% of these men would be considered to be normally fertile. I concluded that either the standards were too high or else there was some "X" factor in male fertility that we did not understand. Unfortunately this "X" factor was not the enzyme hyaluronidase, though

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it may be the physiological vigour of the sperm population. Since that time it has become increasingly obvious that our standards of normality were too high. Macleod (1953) of America now considers that 20,000,000 sperm cells per cubic centimetre are adequate for fertilization provided that the sperm cells exhibit good, forward, progressional movement. This forward activity I shall refer to in this paper as "good sperm migration".

Retrograde Ejaculation.

The second recent advance in the study of male subfertility is the discovery of a number of men who suffer from retrograde or backward ejaculation of semen into the bladder. No spermatozoa are found in a seminal assay, but spermatozoa may be recovered from the bladder. Such patients present with the clinical syndrome of pseudo-azoospermia. The seminal fluid can be retrieved by means of a catheter (Hotchkiss *et alii*, 1955), and it has been used with success for artificial insemination. Pseudo-azoospermia should be borne in mind in the examination of all males who suffer from apparent azoospermia.

Frozen Semen.

In the United States of America at least four women became pregnant after the use of stored frozen semen; the subsequent babies were normal (Burge *et alii*, 1954). This work opens up a vista of the future when we can establish a "frozen sperm bank". This would be useful for the wives of soldiers, sailors and air crew in the overseas air routes who are often away when their wives are due to ovulate.

Effect of Temperature on Spermatogenesis.

Considerable recent investigation has been made on the depressing effect upon spermatogenesis of elevation of the scrotal temperature. Several years ago Professor Rugg-Gunn (1942) of Sydney demonstrated the same effect in rams. In the case of the subfertile male, inquiry should be made into the temperature of the atmosphere where he works, whether he wears tight underpants, or whether he has a varicocele, which apparently raises the temperature of the scrotum. Dr. Ian Potts has noted improvement in 75% of subfertile males treated by the high ligation of varicoceles (Potts, 1956).

Advances in the Treatment of Subfertile Males.

In the field of treatment much work has been done, but little has been consolidated as a recent advance except for the work on varicoceles. Swyer (1953) of London claims to obtain good results from the implantation of pellets containing 300 milligrammes of testosterone. The indications for this therapy are a moderate depression of sperm cell density or motility. This claim should be investigated by one of our clinics. The so-called "rebound treatment" with the female hormone appears to have come and gone (Heckel *et alii*, 1952). It was originally suggested that if large doses of female hormone were administered for about six weeks, then spermatogenesis was suppressed and subsequently there was a pronounced improvement in the sperm cell count above the level found before treatment. There are some patients in whom no rebound occurs and in whom the sperm cell count remains depressed. Out of 64 men so treated, 13 failed to develop the "rebound" phenomenon and their sperm cell count was worse than before. This raises the question of possible litigation.

Thyroid Extract.

It is now agreed that thyroid extract is useful only if the patient is suffering from hypothyroidism. It is doubtful if hypothyroidism is present in any greater degree among the infertile than among the fertile section of the population (Peters *et alii*, 1948). There is still need for the investigation of the exact significance of a lowering of the basal metabolic rate by 15% to 20%. This lowering of basal metabolism is common amongst Australians; it may be the reason for our national characteristic of leaning against posts.

Vitamin E.

Under the heading of vitamin *E* I wish to report the work being done by Dr. Ian Potts (1956), who supervises the male clinic at the Women's Hospital. He has tried to settle whether vitamin *E* is at all effective. He is performing a controlled experiment, and reports that so far a few patients have benefited, but the results are not predictable and could be attributed to natural variations in semen quality. He does not recommend vitamin *E* as a therapeutic agent.

Vitamin A.

Vitamin *A* is therapeutically effective for the elevating of subfertile sperm counts in rams. In a daily dose of not less than 30,000 units it is frequently successful in the treatment of subfertility in the human male when no other factor can be found.

Antibiotics.

In the field of antibiotics I wish to report the work of Dr. Murray Moyes (1955), Dr. Derby Louden and the clinic on the presence of "bacteria without pus" in the seminal fluid. The presence of these bacteria, especially the colon bacillus, is associated with clumping or agglutination of the spermatozoa. This becomes progressively worse after ejaculation. The factor of clumping is of importance only when the number of cells is originally low. The treatment of this condition is by the administration of suitable antibiotics. There are several other causes of clumping in sperm cells which are being investigated at the present time in America.

Recent Advances in the Study of Subfertility in the Female.

Psychological Factor.

The first recent advance is the recognition that many patients who suffer from subfertility are of a distinct psychological type. They are tense, anxious, frustrated, and possessed by an acute sense of inferiority. They feel that other women can produce babies, but that they cannot do so. It may be stated, therefore, that there is a psychogenic type of sterility. It is still unknown how this is translated into a physiological dysfunction. Utero-tubal spasm has been indicated as a cause, but unpublished work at our hospital leads me to believe that it is not the whole explanation. In the clinic at the Women's Hospital, Crown Street, no woman is accepted as a patient until she has brought in a seminal specimen from her husband. It is noteworthy that 10% of these women become pregnant between the time when they bring in this specimen and the time when they are first examined in the clinic. Some psychological factor may be at work here, for they have all suffered from sterility for at least a year before being enrolled. As Samuel Meaker (1955) states: "A patient is a human being with worries, fears, loves and hopes, and not simply the possessor of a womb that doesn't behave."

The Ovarian Factor in Sterility.

With regard to the ovary and its function, I have selected only three items of recent interest. These are the extended or quantitative use of the basal body temperature graph, wedge resection of the ovaries for the Stein-Leventhal syndrome, and the use of light dosage of X rays for the cure of anovulation.

Basal Body Temperature Graphs.

Basal body temperature graphs have been used for some years to determine the presence or absence of ovulation. They are not accurate to the hour, but they are sufficiently accurate for practical use. The new idea I wish to describe is their use in a quantitative fashion as a rough and ready means of estimating the function of the *corpus luteum* (Simmons, 1955). Evidence is now accumulating that changes in basal body temperature are an indication of progesterone activity in the luteal phase of the menstrual cycle. It is therefore necessary to study carefully this phase of the cycle as represented on the basal temperature graph. The phase should be fourteen days in length,

it should be at least four-fifths of a degree in height on the graph, and the general shape of the graph line should be that of a sustained plateau. Any deficiency in any one of these three basic criteria indicates that a premenstrual curettage should be performed, because in most patients with one or all of these defects in the basal body temperature graph the progestational endometrium will be underdeveloped or will be developed in a faulty manner. Three errors in the physiological maturity of the endometrium may be found as follows: (i) general under-development for the day of the cycle or secretory hypoplasia; (ii) local areas of secretory hypoplasia; (iii) "patchy ripening" of a mixed type of endometrium.

Wedge Resection for Stein-Leventhal Syndrome.

The Stein-Leventhal syndrome consists of the triad of amenorrhœa, hirsutism and sterility due to the polycystic condition of the ovaries (Stein, 1955). When culdoscopy reveals the presence of polycystic ovaries, the operation of wedge resection appears to give good results. In Stein's series of 88 patients, 95% regained their menstrual function and 89% became pregnant. It does not require a statistician to decide that this is a most satisfactory result. These results apply only to those cases in which the syndrome is present; they are not meant to indicate a general onslaught on every polycystic ovary.

Light Dosage Irradiation for Anovulation.

The subject of light irradiation of the ovaries and of the pituitary gland is a vexed one. It has been discussed previously in this meeting and I will therefore refer to it only as a therapeutic measure that you may not care to use. In the clinic and in private practice we have used this treatment in about 100 cases. Of these women, two-thirds menstruated regularly thereafter and one-third became pregnant. None of the resulting infants has been abnormal. Kaplan (1948) of New York has been able to report on the normal babies of the third generation whose grandmothers were treated by irradiation.

The Tubal Factor in Sterility.

In the group of tubal factors I have selected four recent advances—namely, utero-tubal spasm (or the spastic uterus), the kymographic method of recording tubal peristalsis, new media for tubal patency tests, and the use of polyethylene as a plastic splint in the surgical treatment of blocked tubes.

Utero-Tubal Spasm.

Utero-tubal spasm was described as long ago as 1934 by Meaker, but it has been more frequently discussed since (Stallworthy, 1947). The recognition of this spasm has made it mandatory that no patient should be considered to have blockage of the Fallopian tubes until at least three tests for tubal patency have demonstrated a tubal blockage. One of these tests should be done with a radio-opaque medium, and the other two should be carried out with carbon dioxide. Utero-tubal spasm appears to be a cause of ectopic pregnancy. In our series (Grant and Mackey, 1955) the incidence of tubal pregnancy in women who had had tubal spasm was 2·3%. This is much higher than the usual figure of one in 303 in the general community (Schumann, 1924).

The Kymograph.

It has been suggested in South America by Amerigo Stabile (1953) that the kymographic tracing of Rubin does not record tubal peristalsis, but records rhythmic contractions of a sphincter muscle around the interstitial portion of the tubes. Stabile tied or clamped both tubes and inserted a hypodermic needle through the fundus of the uterus into the cavity. An insufflation performed under these conditions produced the same type of manometric fluctuations as are at present said to indicate tubal peristalsis. This work is worthy of further study.

New Media for Salpingograms.

Several aqueous media have been introduced in the last few years for the performance of tubal patency tests; the best known are "Medopaque", "Salpix", "Endografin", "Viskiosol" and "Viscorayopake". We have used them and gone back to the use of non-viscous iodized oil, because our pregnancy rate is better following the use of this medium and it gives better contrast in the follow-up radiographs taken forty-eight hours later. Some of the aqueous media cause severe abdominal pain, and they are all absorbed too quickly.

Polyethylene Tubing for Plastic Operations on Blocked Fallopian Tubes.

The use of polyethylene tubing as a splint after the performance of plastic operations on the Fallopian tubes is a real advance in treatment (Mulligan *et alii*, 1953; Johnstone, 1955). Rock and his associates have recorded an incidence of 38% of patent tubes after cornual implantation, and a 67% incidence of patency after fimbrioplasty. There are several different techniques for this operation. Among other surgical procedures, the operation of salpingolysis has proved itself to be a very successful procedure, and after it 37% of our patients have become pregnant. After all types of plastic operations for sterility, our success rate for subsequent pregnancy has been 23% in about 150 operations on the tubes or tubo-ovarian spaces.

Other Advances.

In this discussion of recent advances in the diagnosis and treatment of the tubal factor I have omitted some recent but unproven ideas such as that of the cortisone treatment of blocked tubes (Kurtzrok and Streim, 1954) and that of injection of the lower cervical ganglion for spastic tubes, because the results of such treatment are too recent to assess.

The Peritoneal Factor.

The formerly neglected space between the ovary and the fimbriated end of the tube has recently received attention as a common cause of sterility (Murray, 1953; Grant, 1955). This "peritoneal factor" produces veils of adhesions over the ovaries and the outer ends of the tubes and prevents the transport of the ovum into the tubes. It may be diagnosed with certainty only by culdoscopy. However, a salpingogram taken in two positions—that is, with the patient prone and supine—will suggest the presence of the peritoneal factor by the persistence of a concentrated local overflow of oil on each side of the pelvis forty-eight hours after the salpinogram was done. Most of these patients have had a previous operation for acute appendicitis, or they have endometriosis, or they have had a septic miscarriage. If the acute appendicitis occurred in the days before penicillin and chemotherapy, or if a drainage tube was used, adhesions are almost invariably present.

Culdoscopy.

In my opinion culdoscopy is a valuable recent advance that has come to stay. We have carried out this procedure in over 200 patients and found unsuspected pathological changes in the pelvis in over half of them. Culdoscopy frequently demonstrates living abnormality when none can be felt on pelvic examination; it is safer, cheaper, quicker and less damaging than an exploratory operation.

The Nidation Factor in Subfertility.

It has been suggested that the defects I have described in the physiological maturity of the progestational endometrium should be referred to as the nidation factor in subfertility. They have been previously described in this paper in the section dealing with the basal body temperature graphs, and to me they represent an exciting recent advance. This nidation factor stems from another recent advance called "dating" of the endometrium. The introduction of a reliable method of estimating the day in the menstrual cycle by histological examination of the progestational endometrium, is a recent and major idea (Noyes *et alii*, 1950). When a capable pathologist examines a piece of endometrium in the premenstrual phase of the cycle he can state to within three days the histological day of that cycle. If the histological day is more than three days behind the actual day in the cycle, then the

condition is described either as secretory hypoplasia or as an inadequate secretory phase endometrium. The membrane is running late in its development and it is immature physiologically. It was on the postulation that some such factor interfered with the nidation of an already fertilized egg that Christie Brown (1948) based his "estrogen-ethisterone" treatment. In my opinion the doses he suggests are too small.

It has been demonstrated that the condition of secretory hypoplasia is accompanied by a low excretion of pregnanediol (Glass *et alii*, 1955). As I have already suggested, suspicion may be aroused that all is not well with the *corpus luteum* (and hence the premenstrual endometrium) by the examination of the basal body temperature chart after ovulation has occurred. One of three types of abnormal pattern may be seen—an abnormality in length, height or shape.

Though it has not been proved that a defective secretory endometrium interferes with nidation, it is a fair assumption that this is so (Botella, 1954; Tyler, 1954; Mazer and Israel, 1951). Treatment based on this hypothesis gives good results (Gillam, 1955), when no other factors inducing sterility are present. We are now engaged on the investigation of this problem at the Women's Hospital.

The Uterine Factor.

There have been relatively few new ideas on the subject of the uterus itself, if we exclude the role of the premenstrual endometrium. However, formerly tentative ideas have now been consolidated. For example, it is now fairly universally accepted that lesser degrees of uterine hypoplasia or the "infantile uterus" are unimportant, provided that both the premenstrual endometrium and the cervix are normal. The causes of sterility lie only in these concomitant defects. In the same way it is now recognized that most patients with uterine fibroid tumours can become pregnant without undergoing the operation of myomectomy if there is no endometriosis present and if the fibroid tumours are not situated in the submucosa. The removal of small subserous fibroid tumours is unnecessary; in such cases the cause of the infertility is some other factor. The same line of approach applies to the mobile retroverted uterus, which causes sterility by interference with sperm cell migration into the cervix, or by the flattening of its own tubes. The fixed retroversion is different, for this is frequently attributable to other abnormalities in the pelvis, especially old sepsis or endometriosis. A so-called double uterus does not cause infertility because it is double but because some other defect is present. On the other hand, the double uterus is a cause of habitual abortion in the second three months of pregnancy.

The Cervical Factor.

The "cervical factor" implies the failure of spermatozoa to pass through the cervix and into the fundus of the uterus. This abnormality of function has been variously assessed as operating in from 26% (Mazer and Israel, 1951) to 70% (Steinberg, 1955) of patients. Recent publications lay increasing stress upon the importance of the cervical factor. In the clinic we always perform a cervical or Sim's test and a fundal or Weisman's test (Weisman, 1941) on each patient. In over 50% of patients we found no spermatozoa in the cervix, but in 10% of these patients there were nevertheless a number of active migrating spermatozoa in the *fundus uteri*. Therefore in our series the incidence of defective sperm cell migration is 40% by both tests and 50% by Sim's test alone. These results are based on over 2000 sperm cell invasion tests carried out on subfertile women. The physiological vigour of the spermatozoa has an effect on their migration, but poor spermatozoa may be aided by the good qualities of the cervical mucus.

Sim's Test.

The essential feature of the Sim's test is not simply motility but a good forward progressional activity of the spermatozoa. The pregnancy rate is about the same with one such active sperm cell per high-power field as with 25 (Simmons, 1946; Williams, 1953). Pregnancy sometimes occurs shortly after a negative result has been obtained in the Sim's test; this may be attributable to the removal of a thick plug of hostile mucus.

Bacterial Flora of the Cervix.

It has now become apparent that the presence of bacteria in the cervical mucus is not as important as we once thought. The bacterial flora often changes in nature from month to month (Buxton *et alii*, 1954).

The Fern Test on Cervical Mucus.

In 1945 Papanicolaou found that if cervical mucus, taken from the cervix at the time of ovulation, was placed on a clean slide and allowed to dry, it would crystallize out into a pattern that resembled ferns. These crystals consist of sodium chloride and they indicate that the cervical mucus is normal and will be receptive to normal sperm cells. Campoz da Paz (1953) discovered that this phenomenon of fern formation depended upon œstrogens. The test enables us to decide whether the lack of sperm cell invasion is due to defective seminal fluid or to a faulty cervix. It is one of the few tests available for allocating the blame, in a childless marriage, between the husband and the wife.

Habitual Abortion.

To be complete this paper should deal in detail with the problem of habitual abortion. However, the published literature on this subject is so extensive that I have decided not to summarize it, and I should like to make only a few quotations. Eastman (1948) writes as follows:

> As the embryologist sits in his laboratory and studies abortuses he will naturally find that a large number of them are defective . . . the implication has been too much in the past that these defective abortuses are usually genetic in character and that the bad product of conception was foreordained at the moment conception took place.

Evidence is accumulating that in many cases abortion may be attributable to environmental fault of some kind or other; the origin of the abortion is not genetic in every case. The study of considerable data obtained from over 200 premenstrual curettages in patients in whom habitual abortion occurs suggest that a defective endometrial environment is a common cause of the abnormality and that the only effective way to treat it is before the patient becomes pregnant. I therefore suggest that the correct treatment of most patients who suffer from recurrent miscarriages is preconceptional. Treatment should not be delayed until the patient has first missed a menstrual period, but should be instituted every month while the patient is trying to become pregnant and until pregnancy is achieved.

There are four other aspects of this subject which should be mentioned. The first is that Joel has recently restudied the question of whether abnormal spermatozoa can be a cause of recurrent miscarriages in the female. He considers that the likelihood is a strong one, but it cannot yet be proved (Joel, 1955; Asplund, 1954).

The second point is that congenital abnormalities of the uterus are at least 10 times as common in women who suffer from habitual miscarriages as in their normal sisters (Grant, 1952). Every woman who habitually aborts should be investigated by means of a hysterogram, because some of these double uteri feel as though they are a single unit on pelvic examination.

Incompatibility of blood groups does not play a part in miscarriages which occur during the first three months, according to the analysis of our figures by Dr. R. J. Walsh (1951) of the New South Wales Red Cross Blood Transfusion Service. Recurrent miscarriages in the second trimester are different; they may be caused by incompatibility of the Rhesus factor.

Fourthly, incompetence of the cervix has recently been stressed again as an occasional cause of habitual abortion in the second three months of pregnancy (Lash and Lash, 1950; Hall, 1956).

MISCELLANEOUS ADVANCES IN THE STUDY OF SUBFERTILITY.

Pelvic Tuberculosis.

Pelvic tuberculosis is increasing in Australia; half of our cases occur in persons who are native-born Australians. The present incidence in Australia is at least one in 200 (Grant and Mackey, 1955). The incidence is about the same in America, but it is higher in Great Britain where it occurs in about 10 in 200 cases (Sutherland, 1950). It is still doubtful whether streptomycin can cure this condition permanently (Walsh, 1951). Pregnancy is rare in patients with tuberculous tubes (Bellingham, 1954). No work has been done in Australia to discern whether this tuberculosis is human or bovine in type.

Ectopic Pregnancy.

A high incidence of sterility follows the occurrence of one tubal pregnancy, and the cause is usually the residual Fallopian tube (Grant, 1953; Rubin, 1947). There is reason to believe that in many cases this damage to the residual tube was not present primarily and that it is a direct consequence of hæmoperitoneum and subsequent infection.

Endometriosis.

Conservative surgery in endometriosis (Mackay, 1954) continues to yield a much better pregnancy rate than if the patients were not treated by operation (30% to 50%).

Conclusion.

In conclusion, I apologize for a multitude of omissions in this paper, because days, and not hours, would be required to examine their many facets. For example, I have no time to discuss one-child sterility and appendicitis as causes of sterility (McBride, 1953), or the sequelæ of the spastic uterus, or the role of traumatic intrauterine adhesions in sterility or abortion (Shotton, 1954; Asherman, 1950). It is to be hoped that most of the recent advances which have been described will prove to be both permanent and factual in the future.

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Reviews.

The Boke of Chyldren. By Thomas Phaire; 1955. Edinburgh and London: E. and S. Livingstone, Limited. 7½" × 5", pp. 76. Price: 7s. 6d.

THIS book is an exact copy, but in modern type, of the 1553 edition of the first book on pædiatrics written by an Englishman and originally published in the English language in 1545. It is reproduced in the original abbreviated form of printed English of the day, and with the original refreshingly non-standard spelling. The text provides some lucid descriptions applicable to diseases at the present day and reveals many interesting views of the social pattern of the sixteenth century. Even the use of such measures as postural drainage receives full recognition, though some of the advice may seem unpalatable by modern standards, such as the way of ensuring the suitability of a wet nurse; yet the precautions are mostly well founded, even if the remedies are sometimes bizarre and pathetically inadequate. Much emphasis is placed on human milk both as a vector of disease and for its curative values. Few true drugs were available and the ætiology of disease was little understood. At the same time, advice on such matters as the treatment after excessive exposure to cold and of infection of the eyes would not go entirely amiss at the present day. Having taken up this book, one finds it hard to put it down until read from cover to cover. The early English and quaint spelling are soon mastered. Despite the obvious sympathy of Thomas Phaire, the sixteenth century must have been hard for the sick child.

Atlas Illustrating the Topographical Anatomy of the Head, Neck and Trunk. By the late Johnson Symington; 1956. Edinburgh: Oliver and Boyd, Limited. 19½" × 12½" box containing 36 plates. Price: £5 5s.

THIS is a first-rate atlas showing in life size horizontal sections of head, neck, thorax, abdomen and pelvis. The decision to reprint the atlas was made in 1954 by the Council of the Anatomical Society of Great Britain and Ireland, of which the late Professor Symington was sometime President. No alteration has been made from the original printing. Every surgeon would find it profitable to own and study this atlas. It demonstrates in a unique fashion the relationship between one structure and another.

Ciba Foundation Colloquia on Endocrinology. Volume IX: Internal Secretions of the Pancreas. Editors for the Ciba Foundation: B. E. W. Wolstenholme, O.B.E., M.A., M.B., B.Ch., and Cecilia M. O'Connor, B.Sc.; 1956. London: J. and A. Churchill, Limited. 8" × 5", pp. 314, with 100 illustrations. Price: 40s.

IN 1942 a colloquium on "Hormonal Factors in Carbohydrate Metabolism" was held under the auspices of the Ciba Foundation and a volume published of the proceedings. Since 1942 a very great deal of work has been done on the internal secretions of the pancreas, and it was agreed that a new colloquium was necessary. This was held in June, 1955. The proceedings of these meetings, now published, contain eighteen papers with discussions by 28 experts from Europe and America. The papers deal with insulin production in the pancreas, its chemical structure, its effects in the tissues particularly in relation to the passage of sugars into cells, and its relation to other hormones. The action of glucagon is also treated fully. The discussions on the papers are particularly valuable, as all the speakers are experts who can readily see the significance or otherwise of statements made.

The papers are of the high standard always seen in Ciba publications. The book is essentially one for specialists and few medical men would get much from it unless they were more than ordinarily interested in the subjects treated.

Currents in Biochemical Research, 1956. Edited by David E. Green; 1956. New York: Interscience Publishers, Incorporated. London: Interscience Publishers, Limited. 9" × 6", pp. 713, with illustrations. Price: $10.00.

TEN years ago the first volume of "Currents in Biochemical Research" was published. This was so well received that another volume has been issued. This is not a new edition but an entirely new work. Thirty-two contributors, mostly in the United States, provided 27 articles in many fields of biochemical research. The contributors are all investigators in the first rank in their special subjects. "The objectives of these essays", as stated in the preface, "have been to communicate to nonspecialists an overall impression of the present status of the significant problems in each field, to point out the broad strategy of current research and finally to speculate on the likely paths of future research."

On the whole these objectives have been well met. Of course there are variations in the clearness of the presentations by different authors, and some of the subjects discussed are difficult to understand if one has not continuously studied them. There has been more progress in biochemical knowledge in the past ten years than in all the time before, and the articles in this book give very full accounts of the present position and future possibilities without too much time being spent over the mechanics of the researches. As is natural at the present time, the action and use of enzymes are considered by many of the authors. Photosynthesis is treated very fully in 40 pages and chemistry and viral growth in 28 pages. Other subjects considered are hormones, protein structure, the structure of insulin, nucleic acids and nucleotides, porphyrins, biochemistry of nerves and carcinogenesis.

The book is absolutely essential for the biochemist and extremely useful to workers in other fields of biology. The physician, wishing to know the present position of biochemistry, would find much to interest and profit him in this book, particularly an article on "Certain Problems in the Biochemical Study of Disease".

Radiology Physics: An Introductory Course for Radiologists, Radiographers and Medical Students. By John Kellock Robertson, M.A., LL.D., F.R.S.C., F.Inst.P.; 1956. London: Macmillan and Company, Limited. 8½" × 5½", pp. 346, with illustrations. Price: 56s. 6d.

THIS book is a useful contribution to the subject of medical radiological physics. While assuming that the student has covered a general course in physics, the author nevertheless recapitulates the relevant elementary principles and develops them in a systematic way. A fairly full range of items is dealt with. On the more conventional side this includes alternating currents, production measurement and control of high voltage, cathode rays, positive rays and isotopes, X-ray tubes, rectifying and amplifying valves, production, properties and measurement of X rays, with some special diagnostic procedures, and natural radioactivity. More recent developments included are acceleration of particles by cyclic and linear accelerators, artificial radioactivity, uranium fission and nuclear reactors. Simple problems and questions appended to each chapter should prove a valuable guide to the student in testing his understanding of the subject.

The subject has in general been developed from elementary principles. However, this has led in some cases to the devotion of too much space to historical developments, for example, control of tube voltage by rheostat, and the 1928 definition of the röntgen. The distinction between dose and absorbed dose is not clearly made, the dose rate being described as the rate at which energy is absorbed by a medium like tissue and the röntgen (after correct definition) equated to a number of ergs per gramme.

The author gives a brief but interesting appendix on the very important topic of radiological protection, quoting some of the recommendations of the International Commission which reported on this matter. Most readers will feel that this section could have been longer.

This book will be a valuable addition to the library of any radiological department, diagnostic or therapeutic, where teaching is practised, and it will be specially useful to candidates studying for post-graduate diplomas in radiology.

Skin Surgery. By Ervin Epstein, M.D.; 1956. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 9½" × 6", pp. 228, with illustrations. Price: 82s. 6d.

BEFORE indicating the qualities or deficiencies of this unusual work it is important to note that, of the 17 contributors, 13 are dermatologists, three dentists and only one is a surgeon. The thesis of the book is that a dermatologist ought to be able to cope with all the removable skin lesions that he sees in his practice. To this end some time is spent on the basic technique of excising a small skin lesion under local anæsthesia, and this is repeated in detail by at least three separate authors in the early chapters.

The emphasis is on "office" surgery, and as long as this is restricted to the excision of small innocent lesions there can be no criticism. However, the extremely casual approach to malignant disease of the skin deserves severe reprimand.

At least half a dozen alternative techniques are presented as suitable for the ablation of skin cancer. These include cautery, electrodesiccation and curettage, "chemosurgery", endothermy and electrocoagulation as well as excision, to the exclusion of radiotherapy in any form.

Perhaps the most nauseating of unscientific methods of interfering with skin cancer is that referred to as "chemotherapy". This amounts to the piecemeal excision of a malignant condition after the induction of partial chemical necrosis with a zinc chloride paste. Each portion nibbled off is sectioned until it appears clear of tumour in all areas. This astounding procedure, more than any other of the techniques described for the "office" treatment of skin cancer, reflects the total failure to appreciate the behaviour of malignant neoplasms and the adaptation of surgery to meet the challenge.

Except for the single chapter by the sole surgeon Pollack, who presents a realistic approach to the treatment of malignant disease from a sound pathological basis, the impression given by this book is that one could pull out skin cancer like weeds from the garden.

The chapters on purely dermatological procedures such as epilation, therapeutic tattooing and dermabrasion are clear and authoritative. One is left with the feeling that the dermatologist with minimal surgical training can treat with confidence most innocent skin lesions. However, the approach shown in most parts of this book to surgery in skin cancer leaves so much to be desired that clearly the trained surgeon must continue to take the responsibility for these patients.

Health Observation of School Children: A Guide for Helping Teachers and Others to Observe and Understand the School Child in Health and Illness. By George M. Wheatley, M.D., M.P.H., and Grace T. Hallock. Illustrations by Barbara Pfeiffer; Second Edition; 1956. New York, Toronto, London: McGraw-Hill Book Company, Inc. 9" x 6", pp. 507. Price: $6.50.

THE subtitle of this book should be noted. It is certainly an excellent work from which all school teachers could derive much help to enable them to appreciate fully the problems associated with their pupils in times of both health and illness. The opening chapter is devoted to details on the art of observing children and is followed by one on the growing child. Then chapters are devoted to the various bodily systems, and at the conclusion of each chapter is a *questionnaire* for the reader to apply as a test to himself, as well as a list of various projects that could be undertaken.

The interpretation of the earliest signs of the acute ailments of children is clearly described, so as to help teachers to know if, for example, *the child is developing poliomyelitis* or appendicitis in order that medical aid may be summoned quickly when necessary. The signs of chronic or permanent disturbances such as myopia, malnutrition and postural defects are also discussed. Besides many drawings, a series of coloured photographs all add to the clarity of the text. The book could be very profitably used by a group of teachers for a series of discussions on the medical aspects that they are faced with in their pupils. All administrators and doctors working in departments of education will also find much instructive information in this valuable addition to public health literature.

The Christchurch Hospital Medical Manual. Edited by C. T. Hand Newton, D.S.O., M.D., F.R.A.C.P., F.R.C.S. (Edin.); First Edition, 1945; Second Edition, March, 1947; Third Edition, January, 1951; Fourth Edition, April, 1956. Christchurch: N. M. Peryer, Limited. 7¼" x 5", pp. 182. Price: 27s. (New Zealand currency).

IT is difficult for a reviewer not living in New Zealand to know for just what purpose such a book as this was written. It is not complete enough to be a guide for all clinical procedures, and most of its 175 pages are devoted to either details of pathological investigations or descriptions of all types of diets. Surprisingly sandwiched in amongst these is half a page headed "Medical Registration", which mentions an initial registration fee and an annual practising fee, but the actual amounts payable are not given. A list of notifiable and infectious diseases is also included and almost two pages are devoted to the subject of radiotherapy.

The introduction states "the hospital acts as a training centre for Nurses, Dietitians and Massage Students, and has an important duty in assisting in the training of Medical Students", so doubtless these groups will be obliged to read the work. Unlike other recent books from the House of Peryer, this book is not laid out well and one topic follows another altogether different without a break of space, and often without a change in type. There will be little use for this book outside New Zealand.

Clinical Laboratory Diagnosis. By Samuel A. Levinson, M.S., M.D., Ph.D., and Robert P. MacFate, Ch.E., M.S., Ph.D.; Fifth Edition; 1956. Philadelphia: Lea and Febiger. Sydney: Angus and Robertson, Limited. 9¼" x 6", pp. 1246, with many illustrations. Price: £6 17s. 6d.

IN this book the authors describe comprehensively the technique and principles involved in all types of clinical laboratory procedures. Gastric and duodenal fluid examinations, stool analyses, hæmatology, bacteriology, blood, urine and cerebro-spinal fluid analyses and the field of toxicology are all well covered, and good sections are included on pædiatrics, blood bank procedures, parasitology and histological techniques. Instructions for technical procedures are detailed, clear and easily followed, and the cross-indexing system is very attractive. The standard of printing, binding and illustration is very good.

The book does, however, suffer from defects. Chiefly, too much material is retained that is out of date in 1956. For examples of this, one may refer to the salivary urea index, the technique given for removing gastric content, the microscopic examination of vomitus, Ewald test meals, the hippuric acid liver function test, the discussions on hypertrophic biliary cirrhosis and nephrosis, and the reference to Bargen's diplococcus in chronic ulcerative colitis. The table depicting "typical hemograms" in the "eight degrees of appendicitis" (page 169) is certainly a legacy from earlier days.

This edition is labelled 1956, but, in fact, there are few references to literature after 1950. Little consideration is given to certain modern and popular clinical laboratory procedures such as fat balance techniques in the diagnosis of steatorrhœa, uropepsin determinations, the secretin test in pancreatitis, and blood volume estimations by isotopic techniques. Filter paper electrophoresis of hæmoglobin is described, yet filter paper electrophoresis of serum, a very commonly used procedure nowadays, is omitted.

The physiological and biochemical background material is not consistently handled, being at times quite elementary and in other sections unnecessarily complex, *as in the discussion on creatine and creatinine metabolism.* Sections on treatment, as of amœbiasis, are quite out of place in a book such as this. In certain sections, *the emphasis seems wrong;* for instance, isotopic red cell survival techniques by the use of C^{14} and N^{15} are certainly not clinical laboratory procedures, and deserve scant mention, whereas Cr^{51} *techniques* warrant more consideration. There are, as is usual in such books, many unfamiliar neologisms such as "cythemolytic", "rubricyte" and "rubriblast", and "gastrosuccorrhea". The coloured plates of bone marrow smears are poor.

In summary, this is an attractively produced and comprehensively compiled book, which is somewhat burdened with too much irrelevant material, and which has not quite caught up with the times.

Synopsis of Gynecology: Based on the Textbook Diseases of Women. By Robert James Crossen, M.D., F.A.C.S.; Fourth Edition, 1956. St. Louis: The C. V. Mosby Company. Melbourne: W. Ramsay (Surgical), Limited. 7¾" x 4¾", pp. 255, with many illustrations. Price: £2 9s. 6d.

THIS synopsis is unusual in that it is well illustrated, of handy size, and well produced on good paper. The first criticism we offer is that it contains too much detail of experimental work, and offers too many conflicting theories resulting from these experiments. This is not necessary for the student, for whom, after all, synopses are mainly written. The chapter on gynæcological examination is very good and well illustrated. Differential diagnosis is also good. Very little operative gynæcology is included. An extensive knowledge of operative gynæcology is not necessary for a student to pass his examinations, but we think that some knowledge of operative procedure would help him to understand gynæcological treatment in general.

The conclusions drawn concerning uterine cancer and its treatment are based on a full knowledge of modern methods and results.

In regard to ectopic gestation the author writes: "Except in tubal abortion the embryo is likely to remain attached to the ruptured tube and to continue growing in its extruded situation." In our experience this is not "likely" to occur. In severe abdominal hæmorrhage following ruptured ectopic pregnancy Crossen writes: "It may be advisable to wait until

the patient can be put in better condition for the abdominal operation." With modern methods of transfusion and shock therapy this may be risky and unnecessary. Patients have died from massive abdominal hæmorrhage before operation can be undertaken. Ovarian tumours are very well described.

This should be a very handy book for the final year student, and also for hospital residents in their early year of training.

Textbook of Clinical Pathology. Edited by Seward E. Miller, M.D.; Fifth Edition, 1955. Baltimore: The Williams and Wilkins Company. Sydney: Angus and Robertson, Limited. 9" x 6", pp. 1237, with illustrations. Price: £6 1s.

THE increase in the scope and range of clinical pathology is shown by the size of this weighy compendium, edited by Seward E. Miller, Medical Director, United States Public Health Service, and Chief, Division of Special Health Services at Washington. It is impossible nowadays for one individual to write with authority on all branches of clinical pathology. The present volume, now appearing in its fifth edition, is a symposium, the contributors being Clarence Cohn, I. Davidsohn, L. W. Diggs, Alex Kaplan, Ralph McBurney, Albert L. McQuown, Albert Milzer, Emma S. Moss and Emmerich Von Haam.

At first glance, this appears to be a good general textbook of clinical pathology, of the type which is found on the bookshelves of every clinical laboratory. This it certainly is, but it is also a most useful reference book for the practising physician. The preface states that "it is designed to give the medical student, interne, resident physician, clinical pathologist and teacher of medicine an authoritative source of information on how to use the clinical laboratory most advantageously". With this end in view, the subject matter has been arranged somewhat differently from the usual pattern in books of this type. This may be illustrated by quoting the titles of the first seven chapters, which deal with the examination of the blood. These are as follows: "Blood Techniques", "Blood Cells and Bone Marrow Examination", "Anæmias, Erythrocytoses, Hæmoglobinurias, and Abnormal Hæmoglobin Compounds", "Laboratory Tests Used in the Diagnosis and Management of Hæmorrhagic and Thromboembolic Diseases", "Diseases Primarily Affecting Leucocytes", "Blood Groups" and "Blood Chemistry". There follow chapters on "Hepatic Tests", "The Assay of Chemotherapeutic and Antibiotic Agents", and "The Diagnosis of Viral and Rickettsial Diseases". The chapters on "The Assay of Vitamins" and on "The Assay of Hormones" have been largely rewritten in this edition. The chapters on medical bacteriology, mycology and parasitology are completely new. The illustrations are numerous and on the whole very good. Some of the colour plates are excellent, notably those showing malaria parasites in thick blood films. In the chapter on blood and bone marrow examination, written by L. W. Diggs, the "rubriblast" nomenclature for red cells is followed, the pronormoblast being described as a "rubriblast", the basophilic normoblast as a "prorubricyte" and so on. This nomenclature is part of a scheme recommended by the "Committee for the Clarification of Nomenclature of Cells and Diseases of the Blood and Blood-forming Organs" sponsored by the American Society of Clinical Pathologists and the American Medical Association in the years 1948 to 1950. These proposed new names for the cells of the red series have not been generally adopted yet. In using them Diggs differs from most hæmatologists of note, as he does, also, in stating that the megaloblast of pernicious anæmia cannot be distinguished from the young nucleated red cells of the normal marrow.

Books Received.

[The mention of a book in this column does not imply that no review will appear in a subsequent issue.]

"The Medical Clinics of North America"; 1956. Philadelphia and London: W. B. Saunders Company. Melbourne: W. Ramsay (Surgical), Limited. Mayo Clinic Number. 9" x 6", pp. 291, with illustrations. Price: £8 2s. 6d. per year in cloth binding and £6 15s. per year in paper binding.

Contains 26 articles by 29 contributors. An effort has been made to include something on every aspect of hæmatology.

"The Drug Addict as a Patient", by Marie Nyswander, M.D.; 1956. New York and London: Grune and Stratton, Incorporated. 8¾" x 5¾", pp. 190. Price: $4.50.

In this book the addict is studied as well as his addiction.

"History of the School of Tropical Medicine in London, 1899-1949: London School of Hygiene and Tropical Medicine, Memoir No. 11", by Sir Phillip Manson-Bahr, C.M.G., D.S.O., M.D., F.R.C.P.; 1956. London: H. K. Lewis and Company, Limited. 9¾" x 7¼", pp. 343, with 31 illustrations. Price: £2 10s.

Divided into two sections: historical and biographical; both are full of interest.

"The Treatment of Fractures", by Lorenz Böhler, M.D.; Volume I; 1956. New York and London: Grune and Stratton, Incorporated. 9½" x 7", pp. 1104, with 1721 illustrations. Price: $6.50.

This is the fifth English edition; 14 have appeared in German, four in Spanish, two each in Russian, French and Italian, and one in Polish.

"The Premarital Consultation: A Manual for Physicians", by Abraham Stone, M.D., and Lena Levine, M.D.; 1956. New York and London: Grune and Stratton, Incorporated. 8¾" x 5¾", pp. 96, with illustrations. Price: $3.00.

A manual devised to guide the practitioner in his talks with those about to be married.

"J.A.M.A. Clinical Abstracts of Diagnosis and Treatment", published with the approval of the Board of Trustees, American Medical Association; 1956. New York and London: Intercontinental Medical Book Corporation with Grune and Stratton, Incorporated. 8½" x 5½", pp. 670. Price: $5.50.

Reprintings of selected abstracts dealing with diagnosis and treatment, arranged under headings of different systems and subjects. The work is provided with an adequate index.

"Terramycin (Oxytetracycline)", by Merle M. Musselman, M.D., with the collaboration of H. L. Davis, Ph.D., and H. W. McFadden, junior, M.D., with the foreword by Henry Welch, Ph.D., and Félix Martí-Ibáñez, M.D. Antibiotics Monographs, Number 6; 1956. New York: Medical Encyclopedia, Incorporated. 9" x 6", pp. 144. Price: $4.00.

Deals with every aspect of the drug, with chapters on its application in diseases of the several systems.

"Dental Health", edited by Professor H. H. Stones, M.D., M.D.S., F.D.S.R.C.S.; 1956. London: Dental Board of the United Kingdom. 8½" x 5", pp. 84, with 62 illustrations, 51 in colour. Price: 10s. 6d.

Intended primarily for school teachers and for those intending to enter the school-teaching profession.

"Venous Return", by Gerhard A. Brecher, M.D., Ph.D.; 1956. London: Grune and Stratton. 10" x 6¼", pp. 158. Price: $6.75.

Intended to survey the field of venous physiology and anatomy since 1937.

"Quantitative Problems in Biochemistry", by Edwin A. Dawes, B.Sc., Ph.D., F.R.I.C., with a foreword by J. Norman Davidson, M.D., D.Sc., F.R.I.C., F.R.S.E.; 1956. Edinburgh and London: E. and S. Livingstone, Limited. 8½" x 5½", pp. 236. Price: 21s.

Designed to prevent students in biochemistry from becoming illogical and imprecise in their attitude to the subject.

"Progress in Hematology", edited by Leandro M. Tocantins, M.D., with 27 contributors; Volume I, 1956. New York and London: Grune and Stratton. 10" x 7", pp. 346, with many illustrations. Price: $9.75.

Designed to allow the clinical and investigative worker to learn the progress made in different aspects of hæmatology.

"The Principles and Practice of Medicine: A Textbook for Students and Doctors", by Sir Stanley Davidson, B.A. (Cantab.), M.D., F.R.C.P. (Ed.), F.R.C.P. (Lond.), M.D. (Oslo), and the staff of the Department of Medicine, University of Edinburgh, and Associated Clinical Units. Third Edition, 1956. Edinburgh and London: E. and S. Livingstone, Limited. 8½" x 5½", pp. 1089, with 73 figures and five colour plates. Price: 35s.

First published in 1952, this book reflects the teaching of the University of Edinburgh.

The Medical Journal of Australia

SATURDAY, NOVEMBER 10, 1956.

All articles submitted for publication in this journal should be typed with double or treble spacing. Carbon copies should not be sent. Authors are requested to avoid the use of abbreviations and not to underline either words or phrases.

References to articles and books should be carefully checked. In a reference the following information should be given: surname of author, initials of author, year, full title of article, name of journal, volume, number of first page of the article. The abbreviations used for the titles of journals are those adopted by the Quarterly Cumulative Index Medicus. If a reference is made to an abstract of a paper, the name of the original journal, together with that of the journal in which the abstract has appeared, should be given with full date in each instance.

Authors who are not accustomed to preparing drawings or photographic prints for reproduction are invited to seek the advice of the Editor.

MEDICAL RESEARCH AND HOW IT SHOULD BE PAID FOR.

By tradition, research is a function of universities, but today, because of the scale on which support is needed, the nature of many of the investigations required, and the need to integrate research policy in general, it has been found necessary in many countries to create a central organization or organizations for the promotion of research.

THESE WORDS are used to introduce the summary of the account of a symposium on the support of medical research,[1] which was organized by the Council for International Organizations of Medical Sciences. This body, which rejoices in the abbreviated name of C.I.O.M.S., was established under the auspices of two other alphabetical bodies—U.N.E.S.C.O. and W.H.O. The symposium was held as long ago as October, 1954, at the Royal Society of Medicine, London, under the chairmanship of Sir Harold Himsworth, F.R.S., who is secretary of the Medical Research Council of Great Britain. This book is not a formal report to any formal body, but "an expression of views of a gathering of persons experienced in matters relating to the support of medical research". The number of persons taking part was 29 and many countries were represented. The bodies organizing the symposium, of course, had representatives; the United States had four representatives and the United Kingdom three. Australia was represented by Dr. R. E. Richards, medical recorder of the National Health and Medical Research Council.

The first meeting was opened by Professor J. Maisin, Chairman of the Executive Committee of C.I.O.M.S., in the presence of Sir William Gilliatt, President of the Royal Society of Medicine, who also spoke. Sir Harold Himsworth then took over the conduct of the meeting. In his opening remarks he insisted that the most important factor in research was the research worker. But medical research workers could not live in a vacuum; they required some sort of structure to support and sustain them. Countries differed in their cultural, social and economic backgrounds; these differences were reflected in the organization for support of medical research. The different ideas about organization of research were differences only of detail. Research workers were all aiming at the same objects and were looking for recruits made of the same stuff. Thus there arise for discussion two subjects—the recruitment of new research workers and the methods by which their equipment shall be paid for and their remuneration provided.

Those who are to work in medical research laboratories should, if possible, be earmarked for their future activities while they are still undergraduates. In the report of the symposium we read that the best students are found in universities which are active centres of research. We would go further and say that all universities should be active centres of research. If they are not, they fail in one of the main purposes of their existence. A university certainly has to teach, but it also has to discover. The student should be conscious of the fact not only that his teacher knows what he is talking about, but that his inquiring mind is still active; in other words, that he is engaged on a research project. Such a teacher will not be content to impart certain facts; his teaching will be such that the student will want to know why, and the teacher will encourage him to try to find out for himself. The teacher, if he does his job properly, and if he is not overburdened with enormous numbers of students, will take note of how the student's powers of observation develop and then how he sets about the process of discovery for himself. He will soon grade his students into those of average and those of superior ability. Those of inferior ability he will reject on the day of examination. Among the more intelligent he will not have much difficulty in recognizing the few with first class minds. Like cream of good milk, they cannot help rising to the top. In the symposium report we read that initial selection for training must necessarily take place before there can be direct evidence of research ability. Those selected will generally come from the ranks of those with superior ability. At this point we may raise the question of who is to do the selecting. Of course, the inclination of the student may lie in a certain direction; there should then be little difficulty. However, that does allow us to raise the question of the appointment of a full-time dean of the faculty of medicine. A dean of the faculty who has his own department to run will have little time to give to the study of each student's attainments or the assessment of his capabilities. The duties of a full-time dean might not be easy to define, but the giving of advice to individual

[1] "The Support of Medical Research." A symposium organized by the Council for International Organizations of Medical Sciences, established under the joint auspices of U.N.E.S.C.O. and W.H.O. Edited by Sir Harold Himsworth and J. F. Delafresnaye, C.I.O.M.S.; 1956. Oxford: Blackwell Scientific Publications. 9" x 6", pp. 182. Price: 17s. 6d.

students would certainly be one of his cares. From time to time in discussions on post-graduate education in these columns emphasis has been placed on the advantage to the budding clinician of a period of service in the laboratory under the guidance of a skilled research worker. There is little doubt that with this beginning some would choose the field of research as their destiny. So far, so good—we have discussed the embarkation of graduates on a research career; they must show themselves worthy of their calling. It has been said—and possibly with some truth—that heads of laboratories, departmental and institutional, keep on their staffs respectable drones who lack the fire of the real investigator. We know that no worker can be expected to make an important discovery as it were at a moment's notice, that he is more likely to add something to an edifice that is being slowly constructed. What is important is that he shall at least show signs of activity of the right kind. Laboratory chiefs presumably make reports on workers to the body supplying the money for payment of workers. The financial heads must accept the onus for any continuing droning.

This brings us to our second point—the supply of the money to pay for research. The report of the symposium sets out the following functions of a central research organization: "To keep the whole field of research under review; to give speedy support to new subjects and extra support for those developing rapidly; to maintain research in fields in which universities have little or no interest and to undertake socially urgent investigations; to support research in non-university institutions; to give expert advice to government; to undertake work inappropriate for universities or local bodies; to arrange collaboration on a national scale; to act as a clearing house of scientific information; to exchange information on an international scale; and to direct research under its own auspices." This is a comprehensive objective, which need not be discussed at the moment. In Australia we have the National Health and Medical Research Council. Dr. Richards told those who attended the symposium that the grant received by this Council had risen from £32,000 *per annum* to £129,500. (The amount is higher now because salaries were raised in 1955—the latest available figure is £150,000.) The Federal Council of the British Medical Association in Australia has asked that the amount of the annual grant shall be increased, but so far this has not been done. At the last meeting of the Federal Council Dr. W. F. Simmons pointed out that the Commonwealth Scientific and Industrial Research Organization received a grant of £4,000,000 a year. He also said that he had often met with the statement that research was carried out at the Australian National University, Canberra, and that this upset some of the demands of the National Health and Medical Research Council. As the Federal Council's representative on the latter body, he took grave exception to this view. Much more deplorable, of course, was the statement reported by the New South Wales Branch, according to which Treasury officials submitted that in considering grants for medical research, account had to be taken of the fact that many students were receiving financial assistance to enable them to enter faculties of medicine as undergraduates. The type of central research organizations envisaged at the symposium was not quite the same as our National Health and Medical Research Council. Our Council gives grants to institutions and their workers and may coordinate and supervise what workers do with the money they receive from it. The word "supervision" does not appear in its objectives, but since by giving grants year after year, often to the same persons, it implies approval of what they have done, it may be said to exercise a supervisory function. It does not of itself carry out any research. Although the set-up envisaged at the symposium was not identical with what we have, we know that if we use our own organization wisely we shall produce results.

Current Comment.

SOME ASPECTS OF PEPTIC ULCER.

PEPTIC ULCERATION remains one of the major problems of clinical medicine. The ætiology of ulceration of the mucosa in the region of the stomach and the duodenum still remains obscure, despite considerable research into the social factors and the causes of the symptoms. F. A. Jones[1] considers that there is little support for psychosomatic factors as the only cause, although emotional trauma, like other forms of stress, is an aggravating influence on progression and relapse of the disease. Jones suggests that at least 20% of patients present with an atypical clinical picture. While the numbers of patients with gastric ulceration remain fairly constant, the numbers with duodenal ulceration in Western countries continue to increase, though in Great Britain the deaths from peptic ulcer remain at about 5000 annually. Peptic ulcer remains predominantly a disease of men, and while gastric ulcer is more frequent in manual workers, the incidence of duodenal ulceration is evenly spread. Surveys have indicated that peptic ulceration is a disease of those with responsible positions, though there appears to be no confirmation of the allegedly high incidence in 'bus drivers. Jones suggests that familial predisposition to duodenal ulcer is probably related to constitutional hypersecretion. Various diseases have been found to be associated commonly with peptic ulceration, though how far these associations are coincidental or attributable to the non-specific stress induced by the original diseases is unknown. However, E. M. Latts, J. F. Cummins and L. Zieve[2] have reported a surprisingly high proportion of peptic ulceration in patients with chronic, diffuse, pulmonary emphysema.

The diagnosis of peptic ulceration relies considerably on the radiological findings in affected patients. However, radiological visualization of an ulcer crater depends to some extent on the position of the ulcer. As J. G. Teplick[3] points out, chronic posterior perforation of a duodenal ulcer, though a fairly common occurrence, is, more often than not, first diagnosed on the operating table. The clinical history helps in making a diagnosis of posterior penetrating duodenal ulcer in many cases. Teplick considers that a particularly valuable radiological sign, in this condition, is the effacement of the *valvulæ conniventes* on the inner aspect of the descending duodenal loop with coarsening of the mucosal folds and with postero-lateral displacement of the descending loop.

The treatments of peptic ulceration are many. Sometimes the decision whether medical or surgical treatment is instituted depends upon the particular interests of the medical adviser. T. G. Miller and D. Berkowitz[4] are enthusiastic about the results of medical treatment of patients with peptic ulcer in the absence of complications

[1] *Ann. Int. Med.*, January, 1956.
[2] *Arch. Int. Med.*, May, 1956.
[3] *Ann. Int. Med.*, May, 1956.
[4] *Acta med. scandinav.*, Supplement 312, 1956.

necessitating surgical interference. Their conservative therapy was of the type familiar in general practice, and they report satisfactory results in 61·2% of a large series of patients. It is to be noted that they obtained much better results in the treatment of private patients owing, they believe, to more continuous supervision by a single physician and to greater cooperation on the part of the patients.

In the treatment of duodenal ulceration by surgical means R. M. Zollinger and R. D. Williams[1] stress the importance of applying individual treatment to ensure the maximal physiological efficiency of the operation. The surgeon should share in the responsibility of the patient's post-operative rehabilitation. A small gastro-intestinal stoma should always be made regardless of the type of operation. If dietary management fails to correct post-operative difficulties, reexploration is indicated. Occasionally a non-β-cell adenoma of the pancreas may be responsible for recurring symptoms of ulceration. E. R. Woodward, H. Schapiro and J. Felts[2] have made measurements of gastric secretion by the use of cation exchange compounds. Hydrogen ions in the gastric secretion release quinine from a quininium cation exchange resin. The quinine is absorbed and the amount is calculated in the urine, so that, indirectly, the quality of gastric secretion can be estimated. The method is as yet of no practicable value in the management of peptic ulcer, but it does reveal the response to vagotomy when this has been performed in cases of marginal ulcer following partial gastrectomy. However, as L. W. Edwards *et alii*[3] have stated, vagotomy as the sole treatment in cases of anastomotic gastrojejunal ulcer frequently gives disappointing results. It is best combined with excision of the ulcer and resection of the pyloric antrum. In cases in which gastric resection has been performed with total removal of the pyloric antrum, vagotomy is the treatment of choice. H. Ogilvie[4] suggests that the remote possibilities of perforation and carcinomatous change, and of major hæmorrhage presenting as a surgical emergency, are not the real indications for operation in cases of gastric ulcer. However, many gastric ulcers which do not heal early by medical treatment recur constantly as muscular activity breaks down the healing tissues in the stomach wall. Moreover, the results of surgical treatment are very good, and it is contraindicated only in the treatment of an ulcer of a young person before trial has been made of medical treatment. To Ogilvie duodenal ulcer is a new disease brought on by the stress of modern life. If the ulcer does not heal, complications of a serious nature are almost bound to occur, so that surgical treatment is usually indicated. The indications for operation in cases of severe bleeding are not the size of the hæmorrhage but the chronicity of the ulcer. When a duodenal ulcer perforates, surgical treatment is aimed not to cure the ulcer but to cleanse the peritoneum. Operation is not indicated when the perforation does not soil the peritoneum. Ogilvie suggests that the complications after surgical treatment are the results of bad surgery. The results of operation in cases of duodenal ulcer "vary from very good to dreadful". Ogilvie concludes with a long list of surgical techniques, some of which are still popular, all of which, he suggests, should be discouraged, and some of which should be banned. A plea for early surgical intervention in suitable cases of chronic peptic ulceration is made by N. C. Tanner,[5] who has found that early and frequent surgery has decreased the mortality from bleeding peptic ulcer and gastritis in a population of increasing age. Tanner operates on the known chronic ulcer patients within a few hours of the patient's admission to hospital, but uses a form of selective intervention if the patient is under the age of forty-five years. If surgery is not instituted on admission of the patient to hospital, he is examined by gastroscopy to determine the cause of the bleeding. This discloses not only the chronic ulcers and neoplasms, but also the small, acute ulcers which could not be demonstrated by radiological means.

A. H. Gosse[1] discusses the incidence of peptic ulceration from the study of the personal insurance statistics of several thousand medical practitioners. It is apparent that in the years after the first insurance claim for peptic ulceration there were many claims for recurrences of the ulcer and for other forms of medical incapacity. From the rather small figures there appeared to be an increase in the mortality rate among doctors suffering from peptic ulcer. The sickness rate among those doctors was greatly in excess of that among the other doctors. In the twenty years since the first diagnosis of peptic ulcer in 52 doctors, none older than forty-six years at the initial claim, there were claims for 14,596 days of sickness, of which only 22% were attributed to the peptic ulcer. The increased sickness was particularly noticeable in the younger age groups. An interesting side point was that doctors with peptic ulcer were not only prone to other sickness, but also more prone to accidents. Perhaps they were also more prone to claim insurance benefit. However, as Gosse states, between the ages of twenty-four and forty-five years one in 600 doctors developed a first peptic ulcer, and three out of every five of these had at least one relapse in the next twenty-five years.

Finally, the prognosis of peptic ulcer has been studied by F. A. R. Stammers.[2] He states that partial gastrectomy is one of the most successful operations practised by the modern surgeon. It restores 75% of ulcer patients to normal health, has a mortality in the larger centres of about 3%, and leaves only 7% of the patients still dyspeptic; some of this last group are temperamentally unstable. Mechanical causes of operative failure are preventible. According to Stammers, there are 600,000 to 700,000 people in Great Britain who are suffering from active peptic ulceration. Of these, 80% are adequately treated by their general practitioners; about 30,000 require in-patient treatment, and annually 15,000 to 20,000 operations are performed for peptic ulceration. Without further comment these figures and findings are sufficient to underline the importance of the expensive disease of peptic ulceration at the present day.

COMPLICATIONS OF MYELOGRAPHY

DESPITE reassurances, uneasiness has persisted in many people's minds about the alleged harmlessness of radio-opaque material used in myelography and not afterwards removed. Myelography is a relatively common procedure nowadays, and its diagnostic value is beyond question. Nevertheless, its complications, if any, should be appreciated. The experience of F. L. Davies[3] is very much to the point. Davies, who writes from the Department of Neurosurgery at the Middlesex Hospital, has reported the results of a follow-up of 119 patients who had undergone 125 myelographic examinations for various diseases of the spinal cord from one to fifteen years earlier. The difficulty was appreciated of blaming the contrast medium for any particular adverse effect; but it was assumed that any new symptom or sign appearing immediately after, or within a short interval of, the injection of the medium was due to that substance, always provided that the technique of injection was correct. This seems rather sweeping unless Davies means to imply that "correct technique" rules out the headache that commonly follows simple lumbar puncture and symptoms of functional origin that susceptible persons may produce after such a procedure as myelography. However, quibbling on this point does not lessen the importance of certain of the findings. In 56 cases immediate reactions followed the injection of the radioopaque material (ethyl iodophenylundecylate). In addition to headache, neck stiffness, nausea, vomiting and giddiness, which were the commonest symptoms and could have been (which does not mean that they were) of functional origin, effects included cranial nerve palsy

[1] *J.A.M.A.*, February 4, 1956.
[2] *Surgery*, May, 1956.
[3] *Ann. Surg.*, February, 1956.
[4] *M. Press*, July 11, 1956.
[5] *Ibidem.*

[1] *M. Press*, July 11, 1956.
[2] *Ibidem.*
[3] *Lancet*, October 13, 1956.

involving the third and fifth nerves and lasting for three weeks, nystagmus lasting for two weeks, pyrexia (10 cases) persisting on an average for ten days and retention of urine (three cases) for up to seven days. Severe pain in the spine and aggravation of symptoms due to an existing condition were fairly common and lasted up to fourteen days. A follow-up study after periods from one to fifteen years revealed certain persistent symptoms. An attempt was made to correlate the symptoms with the position and distribution of the radioopaque material remaining in the subarachnoid space. Davies points out that the limitations of this method are obvious; for, except when operative and post-mortem evidence was available, it was impossible to incriminate the contrast medium with certainty. However, in the cases in which this evidence was available, it was of great interest. Five patients underwent laminectomy a year or more after myelography. In four cases it was the second operation, and in each the arachnoid was found toughened and lined by a tough, sticky, white exudate. The nerve roots were adherent to the exudate, and in one case the nerves of the *cauda equina* were deeply embedded in the thick membrane lining the arachnoid. In another case several loculi containing globules of the medium were found in the subarachnoid space. Unfortunately, Davies does not state what symptoms, if any, were experienced by these patients who underwent operation. Three patients who came to autopsy had all complained of persistent backache and neck stiffness, and one had suffered from severe intercostal neuralgia and an herpetic eruption after the myelography. In all three cases the pia-arachnoid showed changes similar to those found in the patients who underwent operation. One patient, whose basal meninges were thick and opaque, had had severe headaches after the myelography, and radiography of the skull before death had shown globules of medium scattered throughout the basal cisterns.

It is hard to be sure of the significance of many of these findings, but the damage found at operation and autopsy cannot be gainsaid. There seems to be no reasonable doubt, as Davies states, that in susceptible patients the injection of ethyl iodophenylundecylate is not without danger, and special care should be taken when the cisternal route of injection is used. Myelography is a valuable diagnostic procedure, and the practical problem seems to be one of finding a way to diminish its ill effects while retaining its use. Davies supplies the answer, in part at least, when he points out that the large amounts of medium shown by radiography to be present in the cranium many years after injection indicate a slow rate of absorption. This emphasizes the desirability of removing as much of the contrast medium as possible after myelography or at operation. This should diminish the chances of the substances entering the cranium and producing disabling symptoms. A more satisfactory solution, of course, would be the development of a completely innocuous contrast medium.

THE RECONSTRUCTION OF ARTERIES.

ONLY in recent years have the techniques of reconstruction of arteries been widely practised. The development and organization of arterial banks for the preservation of arterial tissue until required already appears to be nearly out of date, and such distinguished workers as C. G. Rob, H. H. G. Eastcott and K. Owen[1] now prefer the plastic prosthesis for arteries of the size of the external iliac or larger. The results are as good, the techniques are easier, and there is less risk to the patient when the plastic prosthesis is used. Fairly long defects can often be repaired by simple end-to-end anastomosis, especially in the long tortuous arteries of the arteriosclerotic. Rob *et alii* have found that the freeze-dried homologous arterial transplant is satisfactory for clinical use. The method is probably the best one for the preservation of arterial tissue. This view is confirmed by the experiments of W. H. Sewell *et alii*,[1] who found that there is less host tissue reaction to the homograft which has been freeze-dried. The freeze-dried graft tends initially to lose its elasticity more quickly than the fresh arterial graft, but stabilization is earlier in the freeze-dried graft, and the eventual structure most closely approximates to the normal. Rob *et alii* consider that the donor should be young, and the material is better removed by an aseptic technique *post mortem*, as measures to sterilize the arteries may interfere with the function. An homologous transplant does not survive, and there is little ingrowth of the host tissue. The function of the graft depends on the remaining elastic fibres. Thus a plastic or other artificial prosthesis should serve at least as well as the homologous graft. Rob *et alii* have found that materials such as "Vinyon", "Orlon", "Nylon" and "Terylene" cloths have definite disadvantages, and they have had the best results with polyvinyl alcohol sponge tubes. In addition, for arteries the size of the popliteal, a crimped silicone-coated chemically treated "Nylon" tube has been used satisfactorily. In the case of coarctation of the aorta a prosthesis is often necessary, not usually because of the length of the stenosis, but because of the presence of an aneurysm. An arterio-venous fistula is best treated by reconstruction, though the operation should be delayed to allow the establishment of a good collateral circulation. Of their series of 36 patients with aortic aneurysm treated by reconstruction, 27 are alive and well. Rob *et alii* suggest that aortic embolectomy may be successfully attempted much later than was originally practised. In the reconstruction of smaller arteries an homologous arterial transplant is preferred, though in experienced hands the autogenous vein graft may give better results.

The experimental findings of A. A. Lazzarini *et alii*[2] are in agreement with those of Rob *et alii* in suggesting that the function of the homologous arterial graft depends entirely upon the preservation of the elastic tissue. The techniques of reconstruction continue to be more ambitious, and R. Warren[3] has even reported the successful use of an homologous arterial graft to bypass an obstructed aorta or iliac artery by use of the blood supply from the divided splenic artery. W. S. Dye *et alii*,[4] two to four years after the insertion of autogenous vein grafts, have noticed some localized aneurysmal dilatation, but rarely any general enlargement. The grafts did not close in properly selected cases with adequate resection of the obstructed segment. In the experimental use of synthetic materials for arterial grafts, R. A. Deterling and S. B. Bhonslay[5] have had good results with the use of "Nylon" and "Dacron" materials, while B. G. Lary *et alii*[6] have, experimentally, had some interesting results using stainless steel wire mesh tubes, and C. Horton *et alii*,[7] using autogenous skin grafts, have successfully repaired defects of the aorta and have noted some interesting histological changes in the graft material. J. A. Schilling *et alii*,[8] again experimentally, have used arterial homografts in the replacement of the renal artery with good recovery of renal function.

An analysis of 120 cases of major arterial grafting in which freeze-dried homografts were used has been made by A. W. Humphries, V. G. de Wolfe and F. A. LeFevre.[9] In most of the cases the angiographic findings before the operation compared well with the eventual outcome of the graft, so that it became possible to predict the likely success of the procedure. Critical evaluation of angiograms must be more stringent in candidates for femoral grafting than in those for aortic replacement. Nevertheless, grafting may save some limbs in which the outflow of blood distal to the site of blockage is potentially poor and

[1] *Brit. J. Surg.*, March, 1956.

[1] *Am. J. Surg.*, March, 1956.
[2] *Arch. Surg.*, January, 1956.
[3] *Ibidem.*
[4] *Ibidem.*
[5] *Ibidem.*
[6] *Ibidem.*
[7] *Surgery*, June, 1956.
[8] *Surgery*, April, 1956.
[9] *J.A.M.A.*, July 7, 1956.

in which there are pre-gangrenous changes. In the series of 120 grafts, 90 have been completely successful. Six patients died as a result of the operation, and six patients died from associated causes. Most of the failures were due to inadequate outflow from the graft and had been predicted.

P. W. Sanger *et alii*[2] consider that the use of arterial homografts presents such difficulties in preparation and storage, and is attendant with such risks of deleterious changes that artificial fibres are more practicable. They have used several synthetic materials and have now come to use knitted grafts of interwoven "Orlon" threads through which there is virtually no seepage of blood in use. There is sufficient elasticity to produce almost normal pulsation, but there is negligible stretch. The material is not coated or stiffened. "Nylon" material has been similarly fashioned. These materials have proved satisfactory for the aorta and common iliac arteries, but the results in smaller arteries have been discouraging. In this field Sanger *et alii* are now investigating the use of "Teflon", a new synthetic fibre which is non-wettable and has no cohesive power *in vitro*. There is little resistance to blood flow, the seepage of blood is negligible, and clotting is minimized. In experimental animals the "Teflon" graft is found to be well lined by intima within six weeks.

SURGICAL REPAIR OF ATOMIC RADIATION INJURIES.

WITH the increasing use of radioactive materials in industry certain occupational hazards, not previously encountered outside medical radiological practice, present themselves. The chief dangers in the handling of these substances by industrial workers are inherent in a failure to understand the potential power of radioactivity, the failure to carry out the necessary, if tedious, precautions in order to avoid contamination, and finally frank carelessness in the disposal of the materials. Fortunately, most of the recent accidental exposures to radioactivity have been insufficient to cause serious effects, but from time to time serious accidents do occur, and there have been several deaths. N. P. Knowlton *et alii*[2] made probably the first report of injuries received by exposure to radiation, and the original cases are now the subject of a further paper by J. B. Brown and M. P. Fryer.[3] During the course of preparation for the first atomic tests at Eniwetok Atoll, a deviation from the prescribed method resulted in the handling of radioactive substances with bare hands or with no more protection than rubber gloves. In this way, four young men were exposed to high dosages of β radiation. The amount received by the hands was unknown, but the thoracic regions received from one to fifteen röntgens of γ radiation; the ratio of β counts to γ counts was about six to one. While the low penetrating power of β radiation ensured that the whole body effect was minimal, the skin of the hands probably received from 3000 to 16,000 röntgen equivalent physical units, and severe radiation burns ensued. The subjects first noticed a tingling and itching sensation at the time of exposure, followed some hours later by slight erythema and œdema. After a latent period of several days there was a secondary erythema with the formation of vesicles and bullæ which dried and desquamated after three weeks, leaving a new layer of thin epithelium. The lesions then entered a chronic stage with atrophy of the epithelium and loss of secondary epidermal structure. Apart from a neutrophilia there were no significant hæmatological changes, and the patients have remained well throughout. Routine burn therapy was instituted with accessory chilling. Eventually, after some weeks, part of the dead epidermis sloughed spontaneously, and *débridement* was performed. Conservative therapy was maintained. A feature of the lesions was their sensitivity to painful stimuli, and some dressings were performed under anæsthesia. Subsequently, areas have been resected and resurfaced with free thick split grafts with good function in every case. No amputation has been required. Since the completion of grafting at the fourth year after injury no serious changes have occurred, and no deep losses have been noted. The patients have been warned to avoid chemical, radiation, mechanical or other trauma. Another patient treated by Brown and Fryer for a destructive cyclotron burn at the end of a finger, suffered an acute secondary breakdown of the healed area when the finger was subsequently injured. Permanent healing has also resulted in an atomic radiation burn of an ankle, for which some grafting was required. As Brown and Fryer suggest, local non-thermal injuries attributable to atomic radiation may be successfully repaired by surgical means, and successful rehabilitation is possible. Nevertheless, the passage of many more years will be required before the full mischief caused by intensive local radiation can be properly assessed.

[1] *Ann. Surg.*, June, 1956.
[2] *J.A.M.A.*, September 24, 1949.
[3] *Surg., Gynec. & Obst.*, July, 1956.

THE SURGICAL TREATMENT OF HÆMANGIOMATA.

THE hæmangiomata represent probably the most common of all congenital abnormalities. They may occur anywhere on the body and are usually small and cause no disability, so that either they are never noticed or treatment is not required. Occasionally hæmangiomata are large, presenting the familiar appearance of a *nævus flammeus* or port-wine stain. This kind grows only with the child and does not appear to affect the actions of the skin. It is thus of cosmetic importance only. It is the strawberry nævus, whose cavernous vessels appear both above and below the skin, which is the important type of hæmangioma. The strawberry nævus may grow in size relative to the rest of the child and in severe cases may cause destruction of surrounding structures. By its position, the strawberry nævus is not usually so important cosmetically as the port-wine stain, but the nævus is an unsightly object, may cause considerable distress to the parents and may present a potential danger if subjected to trauma. Of particular importance is the cavernous hæmangioma which forms an arterio-venous shunt. Many of the small, superficial hæmangiomata subside spontaneously in early infancy. Many treatments have been devised to cause fibrosis of the tumour, including the application of carbon dioxide snow, the injection of sclerosing agents such as sodium morrhuate and the application of X rays or of radioactive substances. All these treatments are successful in selected cases, but occasionally more vigorous surgical interference is necessary. J. T. Mills[1] states that surgical treatment is rarely justified in cases of *nævus flammeus*. Skin grafting produces as much defect as the original lesion. The tattooing method has proved to be useful and cosmetics are often satisfactory if the nævus is small. Mills believes that primary surgical removal is the treatment of choice for the strawberry hæmangiomata. However, in places such as the eyelid, sclerosing therapy is more practicable. Occasionally after treatment, even by radiotherapy, the strawberry tumour may grow rapidly and immediate excision is indicated. The cavernous hæmangioma may also prove resistant to conservative therapy. In such situations as the lip, multiple excisions may be necessary. In cases in which multiple cavernous hæmangiomata of the face form a large diffuse mass, radon seeds can be used effectively as well as procedures involving multiple excisions. Ligation of larger vessels and the removal of muscle tissue may be necessary if a hæmangioma invades these structures, and injections of sodium morrhuate have proved useful in the treatment of lesions involving the buccal surfaces of the cheek and lip. As Mills concludes, the best method of treating each hæmangioma is determined by the close cooperation and study by the plastic surgeon, the dermatologist and the radiologist.

[1] *Am. J. Surg.*, July, 1956.

Abstracts from Medical Literature.

BACTERIOLOGY AND IMMUNOLOGY.

Local Antibody Production in Organs.

I. BATTY AND G. H. WARRACK (*J. Path. & Bact.*, October, 1955) have investigated local antibody production in the mammary gland, spleen, uterus, vagina and appendix of the rabbit. The animals first received diphtheria and tetanus toxoids by subcutaneous injection. One month later a dose of 0·2 millilitre of antigen was injected into the mammary tissue, the spleen, the liver, the uterine wall, the cavity of the vagina or the appendix, while due precaution was taken against loss by leakage of the antigen. Penicillin was also given into the lumen of the appendix. Ten days later, the animals were bled from the carotid artery; the various organs which had been injected were isolated, lightly washed and then ground with sand, and the supernatant fluids were assayed for diphtheria and tetanus antitoxin. The results revealed that there was an increase in the titre of both antitoxins in the mammary gland and in the cavity of the uterus, vagina or appendix. There was also an increase in the antitoxin in the spleen, only if the blood supply was greatly reduced. No increase of antitoxin was found to occur in the liver of rabbits.

Pathogenicity of Bacterium Coli.

S. N. DE, K. BHATTACHARYA AND J. K. SARKAR (*J. Path. & Bact.*, January, 1956) have made a study of the pathogenicity of strains of *Bacterium coli* from patients with acute or chronic enteritis. Twenty fresh stool specimens, in which no ova or parasites had been found, and which contained few pus cells and little mucus, were used as controls. Twenty specimens were obtained from patients acutely ill with diarrhœa, and a further 20 from patients with a history of intermittent diarrhœa. Three strains, of O groups 26, 55 and 111, were obtained from England for comparison. Cultures were tested for pathogenicity on loops of small intestine of the rabbit; for this, one millilitre of a twenty-four-hour culture in peptone water was injected into an isolated section of small intestine. Twenty-four hours later the animals were sacrificed; the loops were examined macroscopically, cultures were made and sections were stained. Some antisera were prepared, and were absorbed for use in testing the strains isolated. Thirteen strains from acute cases, nine from chronic cases and three from controls, produced pathological changes in the rabbit intestine. The segment was distended and congested, and the lumen often contained greyish or blood-stained fluid from which were isolated organisms usually identical with the strain injected. Two strains pathogenic to loops of small intestine had no effect on similar loops of large intestine. The serological tests were not helpful in identifying or grouping the pathogenic strains. Biochemical tests were of limited value: the "methyl red positive" strains all produced indol, the "indol negative" strains all resembled *Bacterium lactis aerogenes*. The fermentation of saccharose and salicin was of use in grouping the pathogenic from the non-pathogenic types. It was found that the animal pathogenicity effect could also be abolished when the inoculum was contained in pH 7·4 broth, rather than in peptone water of pH 8·4.

Preparation of Poliomyelitis Antigens.

J. BAUMEISTER AND C. A. MILLER (*J. Infect. Dis.*, January-February, 1956) describe the preparation of poliomyelitis complement-fixing antigens from infected tissue culture fluid. They used Fulton and Dumbell's technique—that is, overnight fixation, and incubation for thirty minutes at 37° C. before the tests were read. They prepared antigens from cultures of monkey testis, monkey kidney, and other tissues. The most potent antigens were derived from monkey kidney culture fluids concentrated by ultra-centrifugation. They were type-specific in action, and none of them was anticomplementary. However, unmodified antigens were easier to prepare than were concentrates. The optimum growth periods for virus production were shortest for monkey kidney and longest for testis tissue cultures.

Rapid Diagnosis of Poliomyelitis.

J. L. MELNICK, J. R. MCCARROLL AND D. HONSTMANN (*Am. J. Hyg.*, January, 1956) have used the complement fixation test as an aid to rapid diagnosis, in a winter outbreak of poliomyelitis in New York City. Three cases occurred in a building consisting of two wings, with a common entrance hall and hot water supply. The occupants were staff members of a hospital and their families; 38 were small children. Two children and one adult developed poliomyelitis with paresis, within the month of January. Blood and rectal swabs were collected on February 3. Complement fixation tests were performed on the following day, and 14 samples yielded strongly positive results for typed antibodies; within two weeks type I virus had been isolated from four of these. The range of the investigation was then extended to cover the occupants of the whole building, people who had left it during the period, and close contacts. The presence or absence of children seemed to determine the spread of infection; if one child acquired virus, all its siblings appeared to do so. There was 45% of infection among the parents of infected children. Children tended to show complement fixation to a single strain of virus; some adult sera reacted to all three types. Complement fixation tests uncovered almost twice as many infections as virus isolations. The results emphasize the extreme contagiousness of the infection in a group of susceptible individuals.

Complement Fixation Test for Poliomyelitis.

N. J. SCHMIDT AND E. H. LENNETTE (*J. Exper. Med.*, August, 1955) describe a complement fixation test for poliomyelitis. Sera were obtained from patients with central nervous system diseases, and were diluted to one in four or one in eight solutions and inactivated at 60° C. for thirty minutes. The antigens were unconcentrated fluids obtained from infected monkey kidney tissue cultures. Three types were available, as was also normal uninfected tissue culture control fluid. Lyophilized complement was used, and two units per test were employed after titration in the presence of antigen. The hæmolytic system was titrated with one in 30 complement and with a 2% preparation of sheep cells sensitized with two units of hæmolysin in 0·25 millilitre. Serial dilutions of unknown sera were prepared, the antigen and complement were added, and fixation was allowed to proceed overnight at 4° C. The tubes were warmed, the hæmolytic system was added, and readings were taken after fifteen to thirty minutes at 37° C., or when the controls had lysed. This tube technique was applied to the serum obtained from 27 patients considered to be suffering from poliomyelitis. In 23, either a rise in or high stationary antibody level confirmed the diagnosis, three had no detectable antibody, and one appeared not to have poliomyelitis. There was little difficulty in interpreting the tests. The authors discuss the possibility of dual infection of patients with poliomyelitis and other viruses, such as St. Louis encephalitis and Western equine encephalitis, which may be possible in certain parts of the United States.

Penicillin and Streptococcus Viridans Endocarditis.

M. HAMBURGER AND J. CARLETON (*J. Lab. & Clin. Med.*, July, 1955) have recorded the similarity of the bactericidal rates of penicillin for *Streptococcus viridans* from successfully treated cases of bacterial endocarditis, and from cases in which relapse occurred. When the organism is sensitive to penicillin, a relapse rate of 10% to 25% is frequently observed, although alteration in resistance *in vitro* does not appear to take place. To test this observation further, bactericidal growth curves have been determined for five strains from successfully treated patients, and for five strains recovered from three patients who relapsed. The tests were carried out with crystalline penicillin G added to 45 millilitres of brain-heart infusion broth in flasks. They were sub-cultured daily. The results reveal that the number of days required for penicillin to sterilize cultures from patients who recovered was the same as for cultures from those whose condition relapsed. Variations in the number of bacteria set up in the test seemed to influence the time of sterilization; small inocula were killed in two days, large ones in up to eight days. The authors discuss the bearing of this finding on the variability of numbers of streptococci in vegetations, and the ease, or difficulty, with which penicillin penetrates to the bacteria within the structure of the vegetations.

Properdin.

M. A. LEON (*J. Exper. Med.*, March, 1956) has made quantitative studies on the properdin complement system. This component of serum appears to play a part in resistance, and is involved in the reaction between complement fraction C'3 and zymosan, which can be studied

in vitro. Dilutions of test serum prepared under standard conditions are incubated with properdin-free complements, after which residual complement (C'3) is estimated. C'3 is active in the absence of divalent cations, so comparison of added C'3 and unknown serum to hæmolytic systems can measure this residual C'3. The reaction appeared to follow first order kinetics provided zymosan was in excess, and the serum not diluted beyond one in four. The reaction rate was proportional to the temperature. The author discusses the possible difference between the properdin in the living subject and the activity of serum influenced by unknown co-factors *in vivo*. The technique employed in these experiments gives a measure of the available properdin in the serum under test, compared with the total amount present when an optimum amount of a properdin-free serum is added, ensuring the presence of the co-factors. The authors discuss the possible importance of properdin levels in clinical medicine.

New Viral Agents from Tissue Cultures of Monkey Kidney Cells.

R. HULL, J. R. MINNER AND I. W. SMITH (*Am. J. Hyg.*, March, 1956) describe eight new viral agents recovered from tissue cultures of monkey kidney cells, during the examination of hundreds of thousands of monkey kidney cultures in the production of poliomyelitis vaccine. These agents do not type with poliomyelitis antiserum; they may have been introduced from human sources or horse serum used in the nutrient fluid, but it seems probable that they were introduced with the kidney cells. The cytopathogenic effect was different from that due to poliomyelitis virus, it appeared later, and the cells were agglutinated. The titre of such containing cultures was $10^{-2.5}$ in fresh kidney cell cultures. Some were inhibited by normal sera; only a single strain was inhibited by human γ globulin. Some were from cultures of Rhesus kidney, others from cynomolgus kidney. Two strains have been isolated from monkeys with diarrhœa, and as such may have an animal pathogenicity. All the strains except one could be inactivated by formalin in the same time as poliomyelitis virus. It was thought that there need be little concern over the suggestion that live "simian viruses" exist in the Salk type poliomyelitis vaccines.

HYGIENE.

International Aspects of Maternal and Child Welfare.

L. J. VERHOESTRAETE (*Am. J. Pub. Health*, January, 1956) contrasts statistically the problems of maternal and child health between regions which he classifies as developed and less developed by the standard of infant death rate. The figures he uses, derived from the statistics section of WHO, show that one-fifth of the world population live in areas where the infant death rate is less than 50 per 1000 live births, one-fifth where it is between 50 and 100, and three-fifths where it exceeds 100. He shows that the fall in infant and maternal death rates over the last forty years is parallel, but at very different levels in these regions. The higher mortality extends throughout childhood, where it is very noticeable in the one to four years age group, and is due chiefly to gastro-intestinal, respiratory and infectious diseases. It is stressed that breast feeding is the best method of preventing gastro-intestinal diseases in infants, especially with the frequent lack of adequate water supplies. The influence of living standards, in particular nutrition, is clearly shown by the sharp rise in infant and child death rates in the Netherlands in the years from 1943 to 1945. It is suggested that improvement will come from emphasis on specific points such as the supplementary feeding of protein. Mention is made of the shortage of medical personnel in less developed areas. Without figures the author deduces that less civilized areas are not at a disadvantage in obtaining "harmonious" growth of the child to adulthood, and that they should await the deliberations of social scientists, who are continuously reanalysing child-rearing patterns of Western culture, where women are more frequently in need of "professional guidance and reassurance".

Laboratory Services in the Diagnosis of Leptospirosis.

N. HIRSCHBERG *et alii* (*Am. J. Pub. Health*, January, 1956) describe laboratory procedure and a series of results in the diagnosis of leptospirosis in North Carolina. Recently the need for these tests has greatly increased owing to demand, and the authors consider that some cases have been notified as infectious hepatitis. Procedure included the preparation of antigen from, originally, four strains of leptospiræ and the preparation of hyperimmune rabbit serum for control. A wider range of organisms since used has not increased the diagnoses. The isolation of organisms from infected patients was difficult, as was the maintenance of stock cultures. The results of complement fixation tests, useful early in the disease, become negative as the results of agglutination tests become positive. Cross agglutination was common, but with time a dominant strain emerged. Results reveal that in North Carolina, Weil's disease is very uncommon. Positive results from agglutination tests for leptospirosis in cattle and dogs are frequent. Leptospirosis in humans caused mainly by *Leptospira canicola* and *Leptospira pomona* is widespread in a mild form in North Carolina.

Toxicological Investigations on Dimethylformamide.

W. MASSMANN (*Brit. J. Indust. Med.*, January, 1956) has determined the toxic effects of dimethylformamide on a number of animals. This is the only solvent from which it is possible to spin the polymer polyacrylonitrile for the production of "Orlon". Dimethylformamide is moderately toxic to rats, mice, rabbits and cats with an L.D. 50 of 0·14 to 0·37 millilitre per 100 grammes of body weight for rats, depending on the route of application. Death took place up to twelve days after a single dose, and liver damage was the most prominent feature with some accompanying kidney damage. Dimethylformamide does not irritate the skin of mucous membranes, but can be absorbed through the intact skin of the rat. Some is excreted unchanged in the urine. Repeated doses by inhalation showed rats to be unaffected by concentrations up to 420 parts per million, while cats were upset by concentrations of 100 parts per million.

Microorganisms in Citrus Products.

R. VAUGHN AND D. MURDOCK (*Am. J. Pub. Health*, July, 1956) have investigated, from a public health point of view, the significance of microorganisms commonly found in concentrated citrus juice in America. The preparation process is described, and the means taken to keep the product free from contamination during processing are outlined. The authors state that, in addition, flash heating to temperatures ranging from 155° to 185° F. for two to fifteen seconds is commonly used to control internal contamination that exists in fresh, sound fruit. Coliform and lactic acid bacteria, as well as yeasts, have been recovered from the inside of sound oranges. Acetic and lactic acid bacteria have also been found in citrus concentrates. It is concluded that the presence of coliform bacteria is not indicative of any public health hazard, and that microorganisms capable of growing in citrus juice are the most important and logical indexes of sanitation in the production of high quality citrus products. It is stated that Salmonella and Shigella types cannot survive for long periods in the acid environment of citrus juices or concentrates, and that the spores of *Clostridium parabotulinum*, types A and B, cannot germinate, even though they may be present.

Accidental Poisoning.

G. WHEATLEY (*Am. J. Pub. Health*, August, 1956) presents a condensation of five papers on the growing problem of chemical poisoning in the home, on the farm and in home hobbies. The role of official agencies and educational systems in prevention is discussed. Accessibility of drugs and chemicals in and around the home, and adult carelessness or ignorance are considered to be the main predisposing factors. Control measures already taken include legislation to assure adequate precautionary labelling of drugs and pesticides. Measures suggested include increasing accidental poisoning prevention activities by official health agencies and educational institutions. Health agencies are urged to take advantage of many heretofore "missed opportunities" for the detection of poisoning hazards and education of the community. It is stated that education can best fulfil its functions in prevention of accidental poisoning through three basic approaches: (i) prevention of accidental poisoning through adult education programmes; (ii) integration of instruction about accidental poisoning with the school curriculum; (iii) education of prospective parents in the prevention of accidental poisoning, as well as other home accidents.

British Medical Association News.

SCIENTIFIC.

A MEETING of the New South Wales Branch of the British Medical Association was held at the Royal Alexandra Hospital for Children, Camperdown, New South Wales, on June 20, 1956. The meeting took the form of a series of clinical demonstrations by members of the medical and surgical staffs of the hospital.

Congenital Heart Disease.

Two patients who had had Fallot's tetralogy treated by subclavian-pulmonary anastomosis were shown by members of the congenital heart disease clinic.

DR. DOUGLAS STUCKEY first discussed the diagnosis of the condition. He said that cyanosis usually developed early but might not be present at birth. Such children were usually below average in weight and general development, and were slow to stand and walk. Clubbing was usually present and corresponding in degree to the cyanosis. An important clinical feature was the habit of squatting, and that was present in 75% of cases. Examination usually disclosed a systolic murmur and thrill, and the second sound in the pulmonary area was characteristically single. An electrocardiogram showed marked right axis deviation and right ventricular preponderance with prominent *P* waves. X-ray examination showed anæmic lung fields without much cardiac enlargement, and the pulmonary artery shadow was frequently absent. Two out of three children with cyanotic heart disease over the age of two years would be found to suffer from this condition.

DR. DOUGLAS COHEN then presented the two patients who had been subject to surgery.

The first was a girl, aged nine years, who had been admitted to hospital with a history of cyanosis since birth. The child had been fully investigated at the congenital heart clinic and was known to have an effort tolerance of about 100 yards; that was decreasing. On admission to hospital she was found to be a cyanosed small child with marked finger clubbing, a blood pressure of 90 millimetres of mercury, systolic, and 50 millimetres, diastolic, a palpable thrill and a harsh systolic murmur most audible in the second and third left intercostal spaces one inch lateral to the sternal edge. No other abnormalities were detected. Her hæmoglobin value on admission was 20·8 grammes *per centum*. On March 9, 1956, she was subjected to a Blalock type of operation, recovery from which was rapid and uneventful. Within days her cyanosis became less, and when she was allowed out of bed, her effort limit was greatly increased. By the eleventh day her hæmoglobin value had dropped to 16·6 grammes *per centum*. Her murmur changed to that typical of the anastomosis. Two murmurs became audible, one parasternal in the second and third left intercostal spaces, the other about three inches lateral to the sternum, this being a continuous murmur with a short diastolic component. The child was discharged from hospital on March 28, 1956, to return to the congenital heart clinic.

The second patient, a girl, aged fifteen months, had a history of cyanosis since the age of three months, when a heart murmur was noted. She had been in hospital for most of the past six months. She had very frequent cyanotic turns for which oxygen was often required. She could be up for about three hours daily, sitting or lying about, but that seemed to be the limit of her endurance. Cyanosis was very severe when she was crying. On examination she was noted to be a very cyanosed child with considerable finger clubbing. A systolic murmur was audible loudest in the pulmonary area. X-ray and electrocardiographic findings supported a diagnosis of tetralogy of Fallot. On May 2, 1956, 200 millilitres of packed red blood cells were given, which raised her hæmoglobin value from 18·5 to 21·5 grammes *per centum*. On May 11, 1956, a left Blalock operation was performed. Convalescence was uneventful. Since operation there had been a great improvement in her colour and her effort tolerance, and a continuous murmur could now be heard in the left upper part of the chest as a result of her shunt.

In discussing the cases, Dr. Cohen stated that it was preferable to defer surgery until the child was at least four years old whenever possible. However, should the child's condition be deteriorating it was quite feasible to operate at an early age, although the risk was appreciably greater and the result might not be so satisfactory. An anastomotic procedure, of either Blalock or Potts type, was preferred to a direct attack on the heart; it was felt that the latter procedure carried a greater risk since the block was in the infundibulum rather than at valvular level in most cases. It was also pointed out that it was preferable to leave the pericardium intact until such time as it was possible to deal safely with the ventricular septal defect at the same time as the obstruction to the outflow tract. The results of operation as at present performed were in general extremely satisfactory, and the most gratifying improvement in the child's colour and effort tolerance usually resulted.

Congenital Urethral Valves.

DR. M. SOFER SCHREIBER showed a male child, aged eleven years, who had been suffering from congenital urethral valves. The child had been admitted to the Eastern Suburbs Hospital in November, 1955, under the care of Dr. S. E. J. Robertson, suffering from rheumatic fever. Routine ward testing of his urine revealed pyuria, and he was referred to Dr. Sofer Schreiber for investigation.

On questioning it was found that he had always been a bed-wetter, but had no frequency of micturition or wetting by day. His enuresis was not especially frequent, and had lessened. Six years previously he had complained of some difficulty with micturition on and off for about six months. That had been investigated in a hospital for a week, and a diagnosis of nephritis was made, because of the presence of leucocytes, red blood cells, albumin and casts in his urine. He stated that he now had no difficulty with micturition, started his stream easily and did not strain or dribble.

On examination (after his rheumatic episode had subsided) he was noted to be a healthy looking child, but had unpleasant breath. A soft, blowing systolic murmur was audible at the apex, and his blood pressure was 160 millimetres of mercury, systolic, and 100 millimetres, diastolic. His bladder appeared distended, but his kidneys were not palpable. His urinary stream was good and commenced and ended abruptly without dribbling, but was accompanied by definite abdominal straining.

Excretion pyelography showed a definite hydronephrosis of his left kidney and a probable hydronephrosis of his right kidney *plus* dilatation of the right ureter. His blood urea content was 102 milligrammes per 100 millilitres and a urea concentration test showed a maximum concentration of less than 2%. A catheter passed easily into the bladder, and the residual urine was two ounces. Cystography demonstrated a much dilated bladder with a normal rounded appearance of the bladder neck. There was considerable reflux up both ureters, and the dye outlined the dilated ureters and hydronephrotic kidneys. X-ray pictures taken during the act of micturition ("micturating cysto-urethrograms") showed that an enormously dilated prostatic part of the urethra emptied abruptly into a narrow urethra, just above the membranous urethra. The appearance was considered diagnostic of obstruction by congenital valves, which alone could cause obstruction at that site. A congenital stricture was a very much greater rarity.

Dr. Sofer Schreiber went on to say that congenital valves of the prostatic part of the urethra were mucosal folds which were attached to one end (nearly always the anterior end) of the verumontanum, and flared out and were attached to the side walls of the urethra. The valves were so situated that they always allowed an instrument to pass inwards to the bladder between them, but during micturition the urinary flow ballooned them outwards and together; that caused a considerable obstruction to the flow of urine, and occurred in the bulbous part of the urethra. In the other forms of congenital bladder-neck obstruction—Marion's disease and the aparasympathetic bladder (of Swenson)—the prostatic part of the urethra was not dilated.

The valves were thought to be an over-development of the normal mucosal folds found in the region—coupled perhaps with adhesion and fusion of their medial edges. There resulted, of course, gross dilatation of the prostatic part of the urethra above the obstruction, the bladder became enormously dilated and hypertrophied, the ureteric orifices became dilated and incompetent, reflux occurred and the ureters became dilated and elongated, and hydronephrosis and renal obstruction followed. Superimposed upon the obstruction, infection nearly always occurred, increasing the renal destruction.

Dr. Schreiber said that the valves were a very important cause of urinary obstruction in infants, and accounted for most of the fatal cases during the first year of life. Normally the kidneys secreted urine in the fifth month of intrauterine life, and reflex micturition occurred at that

time. If the valvular obstruction was severe the kidneys might be largely destroyed by the time of birth.

However, there were all grades of obstruction, and Campbell had remarked that some patients went on to the third and fourth decade of life before symptoms became severe enough to make them seek treatment. Typically there was straining with difficult micturition from the earliest days of life, but that was often not observed in the infant. It was easy to overlook urinary dribbling causing a permanently wet napkin, and the important thing was to observe that the baby was not constantly wet, that it went for an hour or so between micturition, and that the stream started suddenly without straining and ended abruptly without dribbling. Frequency was not invariable, as the distended bladder and ureters acted as reservoirs, and micturition might be infrequent. Enuresis was a very common symptom, sometimes a dribbling overflow incontinence, sometimes bladder irritability because of infection.

The most important thing in diagnosis was to observe personally the actual act of micturition. It would be noted in the present case that the boy stated that he had no trouble with his stream and did not strain. When he was watched, it was found that he did strain with his abdominal muscles. Later, after his operation, when he for the first time in his life experienced easy micturition, he realized just how much difficulty he had previously put up with. He had naturally enough no standards of normal micturition.

A cystometrogram was not of great help in diagnosis, but gave valuable information about the bladder capacity, about the pressures developed in the bladder and about bladder sensation. A catheter in the bladder was attached to a reservoir of fluid and to a manometer. Fluid was run slowly into the bladder, and a graph was made relating the volume of fluid in the bladder to the pressure inside the bladder. Bladder sensation was recorded, also any emptying contractions and the expressed desire to micturate. Normally the pressure rose to less than 15 centimetres of water, and the capacity was about 250 cubic centimetres. In the present case there was a bladder of great capacity (over 600 cubic centimetres) developing a very high tension (over 50 centimetres of water). The ureteral contractions normally developed pressure of up to 35 centimetres of water; so that pressures above, say, 20 centimetres, inevitably meant dilatation of the ureters, reflux and back pressure on the kidneys.

Whilst the bladder in the present case remained a high tension, high capacity type, it was obviously essential that the child should micturate frequently—say, every two hours—to prevent back-pressure effects.

Urethroscopic and cystoscopic examinations were performed, but no additional information was gained. As Higgins had pointed out, at urethroscopy the valvular folds were hard to identify, as the stream of irrigation fluid tended to flatten them out against the lateral walls. Thus one might stress the importance of simple investigations which could be carried out by any doctor without access to elaborate urological instruments.

Treatment was, of course, removal of the valves. That might be done either by open operation or by transurethral resection. Both the Great Ormond Street writers of "Urology of Childhood" and Robert Gross, of Boston, advocated open operation by the retropubic approach. Campbell advocated transurethral resection, with preliminary indwelling catheter drainage if indicated by poor renal function and infection. Gross advocated preliminary prolonged suprapubic drainage to allow the kidneys to recover function, deprecating catheter drainage as it caused congestion and œdema of the region about the valves, and made the operation more difficult. When renal function had improved and infection had been controlled, open operation by the retropubic approach was employed, the prostatic part of the urethra being opened anteriorly.

In babies up to two years of age, the exposure was improved by cutting the symphysis and separating the pubic rami. In older children that did not help, as any appreciable separation strained the sacro-iliac joints.

The urethra was closed with 0000 catgut sutures, and a rubber catheter was left in place to act as a strut for twelve to fourteen days. Post-operative suprapubic drainage was free and prolonged to allow the bladder to shrink, and to allow a return of competence to the uretero-vesical valves.

In the case under discussion, the operation had been by no means as simple as it would appear. Visability was poor in the region of the valves, as the obstruction was very distal, the valves bulging towards the membranous part of the urethra. A secondary hæmorrhage occurred from the vascular prostatic incision, and infection of the urine with *Bacillus coli communis* resistant to all antibiotics was a problem. After the suprapubic tube was removed the patient was made to pass his water every hour or two, in order to keep intravesical pressure low, coupled with triple micturition twice or more often daily. That was a device to control infection suggested by both Innes Williams and Douglas Stephens.

In the patients with reflux and megaureters, when the bladder contracted, some of the infected urine was expelled into the reservoir of the ureters; and when the bladder relaxed, the urine ran down into the bladder again. Drainage was thus incomplete.

The patient now had a very good stream without straining. His blood urea content on June 7, 1956, was 26 milligrammes per 100 millilitres, and a urea concentration test showed a maximum concentration of 2·6%. He still had hypertension (blood pressure 150 millimetres of mercury, systolic, and 110 to 120 millimetres, diastolic), and had numerous leucocytes in his urine, with organisms which varied in type from time to time according to the antibiotic treatment.

In conclusion, Dr. Schreiber said that the case appeared to be of interest, first, because of the relative rarity of the conditions in a child of the patient's age and, second, because it demonstrated the value of routine urine testing and the importance of a careful examination of the act of micturition in a patient with any story of urinary difficulty or enuresis. Almost any of the multitudinous obstructive or infective abnormalities of the urinary tract might have enuresis as one of its symptoms—perhaps the only obvious symptom—and it was the doctor's job to investigate thoroughly all medical-resistant cases of enuresis to make sure that there was not an organic basis for the condition.

Cretinism.

DR. KATHLEEN WINNING showed two children, both cretins, who had been untreated on presentation.

The first was a girl, aged nine months. She had one brother, a normal child, aged seven years. The mother stated that the child had always been quiet and slow, and took one and a half hours to take her feeding. Her tongue had protruded. She had always been pale and "snuffled". Examination of the child revealed a typical untreated cretin. She was small, with lemon pallor, big tongue, typical facies and umbilical hernia.

The second patient was a girl, aged three years and eleven months. There were no siblings. She was a "slow" baby, who sat up late, walked unsteadily at eighteen months of age and walked well only at two years and six months. When aged three years and eleven months she wore the same clothes as at sixteen months of age. She went to kindergarten and sat and watched. Other children cared for her as if she was a two-year-old. On examination she was noticeably undersized, with typical facies and rough skin.

Dr. Winning showed slides of the children as they appeared before thyroid was given and showed the children after one month's treatment. Great improvement in both had taken place. Thyroid (one-eighth of a grain) was given daily for one week, and that dose was increased by one-eighth of a grain weekly until a daily dose of one-half of a grain was being given. The increase was well tolerated.

DR. BRYAN DOWD, in opening the discussion, said that there were a number of approaches to the problem of dosage of thyroid extract in infancy and childhood. None of them was entirely satisfactory. Talbot, relating the therapy to surface area, had stated that the daily maintenance dose was between 60 and 90 milligrammes per square metre of body surface irrespective of age. Means had related dosage (in milligrammes per day) to age in the following way: two to four months, six milligrammes; four to eight months, 12 milligrammes; eight to twelve months, 18 milligrammes; twelve to twenty-four months, 24 to 45 milligrammes; two to four years, 30 to 90 milligrammes; four to twelve years, 60 to 180 milligrammes. Both those dogmatic schemes implied maintenance dosages which were probably too small in the early months of life.

The pragmatic approach of Lawson Wilkins was preferable. He had suggested commencing with one-quarter of a grain (15 milligrammes) of thyroid extract daily in very young cretins. That dose was increased at about monthly intervals by increments of one-quarter of a grain (15 milligrammes) until the optimal therapeutic effect had been reached. Wilkins graphed chronological age against "developmental age" and varied his dosage according to progress made. "Developmental age" comprised "height age", "weight

age", osseous age (estimated once or twice yearly) and mental age.

Dr. Dowd stressed the need for prophylactic administration of vitamin *D* during the period of rapid growth occasioned by thyroid therapy to prevent the development of rickets. When anæmia was present, iron therapy was nearly always required in addition to thyroid hormone.

Staphylococcal Pneumonia.

DR. D. G. HAMILTON said that staphylococcal pneumonia might be primary or secondary. If primary, it was restricted to infants and young children, and in them ranked as an important cause of pneumonia. The infection came from an infected breast or from the nose, throat or skin of those caring for the baby. If secondary, the disease developed as part of a general pyæmic process or followed some preceding damage in the lung, of which influenza and fibrocystic disease of the pancreas (with lung involvement) were the best recognized. Whether the pneumonia was primary or secondary, certain complications were very prone to develop, and in young children were the rule rather than the exception. They were lung abscess, tension cysts in the lung, empyema, tension pneumothorax and pyo-pneumothorax.

Dr. Hamilton then presented the following case histories.

A child, aged seven weeks, had four days before admission to hospital developed cough, fever and rapid respiration. He had been given penicillin with no improvement. He became cyanosed on the day before admission. On admission he was noted to be an ill baby with no clear chest signs, but rapid respiration, fever and a marked neutrophile leucocytosis. X-ray examination showed consolidation in the upper lobe of the right lung. He was given streptomycin and penicillin. From a laryngeal swab a *Staphylococcus aureus* was grown which was resistant to penicillin. The penicillin therapy was then suspended, and achromycin was given in its place. The streptomycin was continued. He made satisfactory progress, and resolution occurred without complications.

A child, aged two weeks, had been circumcised a week before admission to hospital. The circumcision wound and the umbilicus had become infected, and he had developed skin pustules. The night before admission he was cyanosed and had grunting respirations. He did not appear to be very ill, but had an impaired percussion note at the mid-zone of the left lung. There was a pronounced neutrophile leucocytosis, and an X-ray examination showed consolidation in the upper lobes of the right and left lungs. He was given "Achromycin" and streptomycin and made satisfactory progress despite a few peaks of temperature. The leucocytosis persisted for several weeks, and by the third week an X-ray examination showed a lung cyst in the upper lobe of the right lung. After a further three weeks the cyst had disappeared and the lung lesion was almost resolved.

A child of six months developed pneumonia. Her doctor ordered sulphadiazine, but when there was no improvement in three days, gave "Chloromycetin". After three days there was still no improvement, and she was admitted to hospital. Clinical and radiological examination showed pleural effusion. Her temperature was 103° F. "Chloromycetin" therapy was continued and streptomycin given as well. Her chest was aspirated each day for the next three days and streptomycin injected into the pleural space. From a laryngeal swabbing and from the pleural pus a staphylococcus, sensitive to all antibiotics, was grown. In three days her temperature was normal, and no more fluid accumulated in her pleural cavity. She made good progress, but an X-ray examination of her chest after a week revealed a ragged abscess cavity in the lower lobe of her right lung. Administration of antibiotics was therefore continued for almost three weeks. The child steadily progressed. The abscess cavity gradually closed in, but some infiltration at the right lung base was apparent radiologically for about two months. This subsequently cleared completely.

A child, aged six months, developed a cold six weeks before admission to hospital. After two weeks she developed fever and rapid respiration. She was admitted to a country hospital and given "Achromycin" with a good response, but after a few days she became worse, distressed and cyanosed. An X-ray examination of her chest showed a pneumothorax. She was therefore transferred to the Children's Hospital, and on admission was distressed and cyanosed with rapid grunting respirations. X-ray examination of her chest showed a right pneumothorax with a small amount of fluid present and some displacement of the mediastinum. "Achromycin" was given and continuous suction aspiration of her chest was carried out with relief of her distress. Within a few hours of the needle being removed from her pleural space, the pneumothorax had recurred, and so continuous suction was carried out for a further twenty-four hours. She remained well and afebrile for eleven days, but then again became collapsed and cyanosed, and her breathing became distressed and grunting. X-ray examination again showed a marked tension pneumothorax. Again continuous suction aspiration of the pleural space was carried out for twenty-four hours with good relief of her distress. Once again after the needle was removed distress occurred, and aspiration was continued for a further thirty-six hours. After that she made good progress despite a few peaks of temperature. Slight residual pneumothorax remained, but this slowly disappeared, and the child made a complete recovery. A staphylococcus sensitive to all antibiotics except penicillin was grown from a laryngeal swabbing.

A child, aged nine weeks, developed a discharge from the left ear one week before admission to hospital. Four days later she became very ill with fever, loss of appetite and impetigo of the scalp. She was given penicillin. She became listless and quiet, but still feverish, refusing food. On admission to hospital she was cyanosed, collapsed and grunting, with a stiff neck, a discharging ear and cellulitis of the scalp. There were pustules on the buttocks. She was extremely ill. A diagnosis of septicæmia and meningitis was made. Lumbar puncture revealed 17 leucocytes per cubic millimetre, a protein content of 20 milligrammes per 100 millilitres, a chloride content of 740 milligrammes per 100 millilitres and glucose present in her cerebro-spinal fluid. X-ray examination of her chest showed a large tension pneumothorax. Blood culture was carried out, and she was given "Chloromycetin" and penicillin in very large doses. The chest was aspirated by continuous suction, and a small amount of pus was obtained from it. From her blood, the ear discharge, pus from her chest and pus from her scalp when it was opened a couple of days later a *Staphylococcus aureus*, resistant to penicillin but sensitive to other antibiotics, was grown. When these sensitivities were determined, administration of penicillin was suspended and "Chloromycetin" given in its place, the "Chloromycetin" therapy being continued. By the sixth day she had made good progress, but some pneumothorax had persisted. By the fourteenth day her temperature was normal, but administration of antibiotics was continued. A transfusion was given because her hæmoglobin value had fallen to 8·8 grammes *per centum*. Steady progress was made, but by the end of the fourth week X-ray examination of her chest revealed a large, air-containing cyst in the lower part of the left lung. This cyst gradually disappeared, and the child made an uninterrupted recovery.

A child, aged six weeks, was weaned because the mother had a breast abscess soon after the child was born. The baby had had a cough since birth, but it had been worse in the last week and the child had been vomiting. On the day of admission to hospital she suddenly collapsed. She was given "Coramine" and oxygen at a district hospital and then rushed to the Children's Hospital. On admission to hospital she was pale, limp, gasping and almost dead. She was given "Coramine" and oxygen, and her airway was cleared through a laryngoscope. Her respirations were rapid and shallow; she was febrile and extremely ill. Clinical and radiological examination suggested consolidation or fluid in the whole of the right side of her chest. It was felt that she was too ill at that stage to attempt aspiration. She was given "Achromycin" and streptomycin and made a steady improvement, her temperature becoming normal in three days. She continued her good progress until the seventh day, when her temperature began to rise again. The chest was therefore aspirated and no fluid found. Next day the chest was aspirated again, and two millilitres of thick pus were obtained. Her condition became worse. An X-ray examination showed a large pneumothorax with adhesions in the mid-zone holding the lung to the chest wall. Her condition rapidly deteriorated, and she died. Post-mortem examination revealed a thick purulent fibrinous exudate covering the whole of the surface of the right lung, extensive pneumonia in the right lung and a broncho-pleural fistula. It also revealed that the child was suffering from fibrocystic disease of the pancreas. From the exudate in her pleural space a *Staphylococcus aureus*, sensitive to all antibiotics, was grown.

Dr. Hamilton made the following comments. First, the case histories represented the typical course of staphylococcal pneumonia in infancy. Second, examination of a laryngeal swabbing taken while the infant was coughing was a useful way to find the organism causing pneumonia in an infant. Third, in sick infants with pneumonia antibiotics should be given generously. Fourth, complications could usually be treated conservatively—tension pneumo-

thorax by continuous aspiration and empyema by aspiration and instillation of antibiotic. A lung abscess usually drained spontaneously into the bronchi or pleural space, and air cysts rarely needed treatment.

Out of the Past.

In this column will be published from time to time extracts, taken from medical journals, newspapers, official and historical records, diaries and so on, dealing with events connected with the early medical history of Australia.

AN APPOINTMENT TO A LUNATIC ASYLUM.[1]

[Thomas Campbell to William Bland.]

Secretary's Office,
Sydney,
12 Sept. 1814.

SIR.

1. His Excellency the Governor having been pleased to appoint you to act as Surgeon to the Lunatic Asylum at Castle Hill, you are hereby directed to assume and take upon yourself the Medical Duties at that situation accordingly cooperating with Mr. Suttor the Superintendent, in the care, management and proper humane Treatment of the unhappy persons placed under your charge with a view to render their Situations altogether as Comfortable as their unfortunate Circumstances will admit of. Herewith you will receive for your Information and Guidance a Copy of the Governor's Instructions to Mr. Suttor with whom you are requested to Cultivate a good understanding.

2. You will be supplied from time to time with such Medicines, Medical Stores, and Comforts, as you may deem essentially necessary for the use of the Lunatics by making a written application for them to D'arcy Wentworth Esq., the Principal Surgeon at Sydney.

3. You will be required to transmit monthly written reports to His Excellency the Governor of the Number and State of Health of the Lunatics and whether any are likely to recover.

4. His Excellency the Governor is pleased to grant you and Your Friend Mr. Randall Permission to Cultivate some Government cleared Ground at Castle Hill lately occupied by a man of the name of Grannano, for your mutual Use and Benefit, so long as you shall continue to Act as Surgeon to the Lunatic Asylum.

I am Sir &c.,
THOMAS CAMPBELL Sec.

Note by Lachlan Macquarie:

P.S. Mr. Bland will commence his monthly reports of the Lunatics to the Governor on the first of the next month of October.

[1] From the original in the Mitchell Library, Sydney.

Correspondence.

MEDICAL OFFICERS AND THE ARMED FORCES.

SIR: I desire to draw your attention to offensive advertisements which appear from time to time in the pages of THE MEDICAL JOURNAL OF AUSTRALIA, namely, those of the Royal Australian Navy and the Royal Australian Air Force, calling for medical officers required respectively to be of "pure European descent" and of "substantially European descent".

Australians abroad are not infrequently embarrassed by questions regarding the "White Australia" policy, the existence of which we refute and attempt to explain away euphemistically as a policy of economic protection. Even this weak refuge is now denied us by the advertisements quoted, for surely they do not carry the implication that British doctors of "non-European" descent would constitute an economic threat by virtue of a willingness to accept lower pay or standard of living than their colleagues of "European descent". The inference to be drawn then is that the reason for exclusion is gross and archaic prejudice. Not only is it intolerable that some of us should have to suffer this indignity, but in a broader view it is a crime against humanity and all ordinary decency, besides exposing Australia to ridicule and contempt.

Is it to be our lot to have thrust upon us *apartheid* in the Services with its humbug of separation of blood for transfusion according to ethnic origin? This will not be dismissed as fanciful if we reflect upon recent events around us. Nor is it a matter for apathy.

As it is unlikely that mere exhortation would bring about the abolition of this iniquitous imposition, it seems proper that we should make our disgust felt strongly. It is earnestly suggested that you, sir, refuse to continue to publish the advertisements in their present form and that aspirants to a service career should confine their enlistments to the Royal Australian Army Medical Corps, unless and until there is a change of heart by the Royal Australian Navy and Royal Australian Air Force. Further, since it is likely that even now some members of the British Medical Association are affected by this discrimination, it might be the duty of that association to take the matter up with the Services concerned.

Yours, etc.,

Fairlight, K. H. S. COOKE, M.B., B.S. (Sydney).
New South Wales.

Temporary address: Corellistraat, 9, Amsterdam, South, Holland.

October 22, 1956.

RAUWOLFIA SERPENTINA.

SIR: Recently certain advertising literature from a manufacturing chemist has contained a solemn caution prominently displayed that products of *Rauwolfia serpentina* should not be used in the treatment of hypertension in pregnancy because "there is some evidence to show that Rauwolfia therapy can cause a serious nasal obstruction at birth, regardless of whether the expectant mother suffered this side effect or not". No authority for this statement is quoted. This is not in accordance with our experience at the Royal Women's Hospital, Melbourne, or in private practice. On the contrary, drugs of the Rauwolfia group have proved of the utmost value in the management of hypertension during pregnancy, and no troublesome effects upon the newborn infant have been noted. In the course of routine consulting I have been surprised at the extent to which this caution has been accepted, and I write this letter for the information of doctors practising obstetrics, lest a drug of real value in the ante-natal care of hypertensive women should fall into disrepute for no adequate reason.

Yours, etc.,

W. McI. ROSE,
Honorary Physician, Royal Women's
421 St. Kilda Road, Hospital, Melbourne.
Melbourne,
October 26, 1956.

ETHICS.

SIR: It is quite obvious that the imprecations of the Victorian Branch Council of the British Medical Association regarding ethical behaviour between members of the profession have gone unheeded, and, whilst this is regrettable from the point of view of good manners, I think that it should be brought to notice that such disregard carries with it a more materialistic repercussion; I refer to the vexing problem of litigation to which unethical members, by their behaviour, expose themselves and their colleagues.

It is fortunate that, up to now, our patients have not been at all "litigation-conscious"; otherwise, judging from what happens elsewhere in the world, I feel sure that we would have witnessed some unedifying and unhappy cases, and my purpose in writing this letter is to bring this aspect of ethics to the minds of the profession. I cannot help but think that the ethical code has assumed its present form as a result of the sum of experience of generations of practitioners from earliest times onwards, and I am convinced that we cannot continue to ignore that experience without the possibility of expensive reminders of its wisdom.

Yours, etc.,

B. S. ALDERSON.
Camperdown,
Victoria,
October 29, 1956.

Obituary.

ROBERT SCOT SKIRVING.

ON July 15, 1956, Robert Scot Skirving joined, as he used to say (in quotation) of certain others who predeceased him, "that choir invisible whose music is the gladness of the world". He was in the ninety-seventh year of his age, and though his latter years had been somewhat difficult to him because of his great age and he himself freely said that he had lived too long and "cumbered" the earth, those who knew and loved him did not expect him to fail in health and die as quickly as he did. As a matter of fact he had planned a dinner party at his home in honour of a distinguished overseas visitor for the day on which he died. He was one of the wisest, most lovable, picturesque and cultured of men and was unique in many respects. His death marked the end of an age-period of medicine in New South Wales. He was the last link with nineteenth century medicine in that State—had he not practised in Sydney in the 'eighties and written lively accounts of what he then saw and did? And what is more, had he not kept alive his interest in medicine and applied the newer knowledge in his practice? He saw patients, who would consult no one else, until a few weeks before his death. But let us look at the life history of this remarkable man.

Let us begin with the name Skirving. In the address which he gave at Robert Scot Skirving's funeral service in Saint Stephen's Presbyterian Church, Macquarie Street, Sydney, Dr. George Bell gave an account of Skirving's career and began by saying that the name Skirving was probably derived from "Scrivener", a writer. However, it is thought that Skirving is simply an Anglicized form of the French *écrivant*—"s" in English often takes the place of an "é" in French, and "k" and "c" are the same; "ri" could very easily be transposed to "ir", and the English "ing" is equivalent to the French "ant". The name Scot came from Robert Scot Skirving's paternal grandmother, who was Margaret Scot. After the marriage of the grandfather the family became Scot Skirving. Among Robert Scot Skirving's ancestors was Black John Skirving, of Plewland Hill, the bearer of the Standard of the Earl Marshal of Scotland at Flodden on September 9, 1513. He escaped with the Standard wrapped around his body and brought it to Edinburgh, where it now hangs in the Advocates' Library. Another member of the family, Adam Skirving, was the writer of the poem "Hey Johnnie Cope"; he wrote songs, mostly Jacobite, and actually saw the battle of Prestonpans in 1745. Still another was Archibald Skirving, the famous artist, many of whose paintings hang in the Edinburgh Art Gallery. At the risk of producing something more like a biography than an obituary notice, it is necessary to give some details of the family circle into which Robert Scot Skirving was born. He was born at Campton, near Haddington, East Lothian, Scotland, on December 18, 1859. There is no doubt that the early years of austere religious upbringing which he had to endure had a constant influence throughout his long life. Not that he adhered to the austerity—the differing avenues of his life saw to that. His early years helped to form his character (as they do with all men), and it is character which is of fundamental importance whatever course of life is followed. In a family record which he wrote, Skirving explains that his paternal grandmother, "a hard old woman who lived in a good house she owned in the main street of Haddington", insisted that her grandchildren when they reached the age of six or seven years should live with her during the week and go home from Friday to Monday. This they did—and it was "pretty horrid". When the grandmother died the children went home to live and rode on ponies to school in Haddington. They were taught by "an admirable old-world typical Scotch Dominie", a Mr. Haig. On Sundays before the grandmother died the family drove in the carriage to church at Haddington. They had luncheon with "Grannie"; the parents went home and left the children to go to afternoon church. After church was over the grandmother's maid taught them psalms and spiritual songs. The maid was "a pretty girl" and a good Calvinist, who did her best to make her young charges be the same. One day when "Maister Robbie" was saying his hymn, the maid looked out of the window and saw a friend. She cried: "Stop, stop, there's Mary Maclean oot, wi' her lad, and wi' a braw new ribbon in her bonnet—and on the Sabbath tae. My wor-r-rd, she'll burn for this some day." These days it is a little difficult to understand such points of view.

From the school at Haddington Robert Scot Skirving went to Edinburgh Academy and from here (he had already acquired a love of the sea) he went to Eastman's Royal Naval Academy in Southsea, near Portsmouth. He succeeded in passing the examinations qualifying him to enter the Navy, only to learn that he was too old by three weeks to be allowed to join. Thwarted in this endeavour, he turned to the Merchant Service, which was not held in such high favour as the Navy. To begin with, he made two voyages to Iceland in a vessel of 700 tons. After this he was accepted as a cadet on the Merchant Service training ship *Conway*. At the time of his death he was the oldest living "Conway boy". Dr. George Bell tells us that John Masefield, poet laureate, is another old boy from the *Conway*. The training which Skirving had received at the Academy near Portsmouth stood him in good stead, and before long he was a main topgallant yard man. In after years he wrote that never before or after had he been so simply happy and contented as he was on the *Conway*. The next thing that happened was an apprenticeship on a "smart little ship", *Tantallon Castle*, of between 1000 and 1250 tons. She sailed for Port Adelaide, and Robert Scot Skirving had his first sight of the island continent which was to become his home and on whose medical destinies he was to shed lustre. But, of course, he had no inkling of this. On the way back to Britain via Cape Horn he became ill with beriberi and was landed at Queenstown. Shortly afterwards he found his way back to Scotland. It was then clear that he must leave the sea. But what to do? His father suggested that he should study medicine, and after working very hard at his entrance examinations, to use his own words, he "fell in love" with medicine. He graduated fifth in his year with second class honours, having missed the first class by one mark. At the head of the first class list was Thomas Peter Anderson Stuart, who was later to found the Medical School of the University of Sydney. After graduation Skirving applied for one of the six posts of house physician. For this he (and others) had to face examiners; he was one of those who were successful. Of course, he was overjoyed, but he was informed that he would not be allowed to take up the position because on the day of registration he would still be under the age of twenty-one years. The examiners solved the difficulty by promising him in advance one of the positions for the following year and suggesting that he occupy the intervening twelve months by study abroad. This does not sound as though it would meet with the approval of the next year's graduates and no doubt it did not; but our new graduate accepted the suggestion and studied in Dublin and Vienna. He thus had two novel experiences—he had been a few days too old to be allowed to enter the Navy and now he was too young to be accepted for registration in medicine. All the same he came back to Edinburgh. He served among others with James Spence, Professor of Surgery, of whom he often told a story against himself. Skirving, seated in the top gallery of the lecture room, fell asleep in the middle of a lecture. Spence stopped and called loudly: "Come down, Eutychus." The class, recognizing the biblical reference, roared with delight.

We come now to the time of Robert Scot Skirving's journey to Australia. He came as surgeon of the emigrant barque *Ellora*. The tale of this journey is an epic and has been told by him in an article published in this journal at the special request of the Editor in the issue of June 27, 1942. After taking up some work as *locum tenens* in Queensland, he accepted the offer of Professor Anderson Stuart to become medical superintendent of the Prince Alfred Hospital. This he did in November, 1883, and held the position until June, 1884. It was here that he met his future wife, Lucy Susan Hester, who was a nurse at the hospital. In 1884 he started private practice at College Street, Sydney, and on his marriage in 1885 he moved to 221 Elizabeth Street.

In 1883 Skirving was appointed honorary assistant physician at Prince Alfred Hospital, and he held this office until 1889, when he became honorary physician. He remained honorary physician until 1911 and joined the consulting staff in 1912, remaining honorary consulting physician until his death. Most remarkable was his simultaneous association in the early days with Saint Vincent's Hospital. Here he joined the surgical staff, becoming honorary surgeon in 1889 and retaining the position until 1923. Such a happening would not, of course, be possible at the present time, but many of his old students will recall the days when he was senior physician at one metropolitan hospital and senior surgeon at another. His knowledge was vast and his enthusiasm and energy were the envy of his students. Sometimes he was ill at ease, suffering the distress of sciatica, but whether he was well or ill the classes of students to whom he taught clinical medicine did not suffer. The students would be seated up to 38 in number around a bed

and he would teach, sometimes with the aid of diagrams on a blackboard, generally with a personal story appropriate to the disease under investigation, and always with serious discussion, all in impeccable English delivered with histrionic and unforgettable force. It is little to be wondered at that when, during the second World War, lecturers were overbusy or scarce and Skirving was asked to give clinical talks at what was now the Royal Prince Alfred Hospital, the lecture hall was filled to overflowing—the attraction of the Old Master never failed. The hospital stood greatly in his debt, and all concerned with the running of it were aware of this. We recall with pleasure the reception held in his honour in May, 1955, when Sir Herbert Schlink, Chairman of Directors, spoke with great appreciation of the long years of selfless devotion given at the institution by Skirving to the practice and teaching of clinical medicine.

As a consultant he was wise and discerning. He always left his general practitioner *confrère* with a feeling that he had received real help. Sometimes he was a little disconcerting for the relations, as on an occasion when he placed a sympathetic hand on the shoulder of an anxious husband and said: "My dear sir, we must not be as those that are without hope in this world, for then are we of all men most miserable." Then with the greatest kindness he gave reasons for the hope that he held for the patient. The husband was impressed and grateful and the hope was justified. If by any happy chance the patient came from Scotland, Skirving was more than pleased and showed it in his whole demeanour.

Skirving served in the South African war with his friend Sir Alexander MacCormick. This episode in his life could fill a whole chapter, but it must be passed by. In the first World War he served with distinction, being surgeon-in-charge of the census division at Queen Alexandra Military Hospital, Millbank, London. It was at about this time that his son, Archie, was killed on active service. The son's death was a cause of great grief to Skirving and had a most profound and enduring effect on his wife's health. When the war was over he came back to Sydney and resumed his practice, but he found life much more difficult than it had been. Many persons, of course, felt this. We know now that what was called peace was no real peace, and that this "intermezzo" in which values seemed to be changing on every hand, unsettled the minds of men everywhere. Skirving's loss of his son and the continued indisposition of his wife were additional loads that he had to bear. His work went on. In due course the Royal Australasian College of Surgeons came into being (it was first known as the College of Surgeons of Australasia) and he was a Foundation Fellow. Later the physicians who had been an "Association" became The Royal Australasian College of Physicians and Skirving became a Fellow. He was proud of this dual Fellowship. It should be recorded that no special function was held, or special visitor was received, by the College of Physicians without a special invitation being sent to him that he might do honour to the occasion. Here it may be mentioned that in 1953 the Royal College of Surgeons of England honoured him by electing him a Fellow. Skirving was always a "good B.M.A. man". He was president of the New South Wales Branch in 1891-1892, and in the year 1935 he completed fifty years of membership and was *ipso facto* absolved from paying any further subscription. He held offices at medical congresses throughout his long life and gave many addresses. His after-dinner speeches were always awaited with eagerness and those present were never disappointed. One appointment which was of value to the community was that for many years he was Chief Medical Referee to the Australian Mutual Provident Society. He himself once expressed the opinion that the appointment did not do him much good, but it was commonly reported that he had a liberalizing effect on the rules for the acceptance of proponents.

THE MEDICAL JOURNAL OF AUSTRALIA owed much to Robert Scot Skirving. He was a constant friend and critic. His criticisms were always valuable and he took a great deal of trouble in making them. If he thought that the occasion warranted it, he would call on the Editor at morning tea time, climbing the two flights of stairs without difficulty. On these occasions he was always punctilious in his personal greetings to every member of the office staff. He was delighted when a review was published of a small book which he wrote on wire splicing. It has been reprinted, and he said once that it was the only thing that he wrote which brought him any money.

Mention must also be made of Skirving's membership of the body known as the Ancient Mariners. Having received some training in the *Conway* and holding a master's "ticket", he was one of the more self-respecting and respected "square rigged" members; those who had qualified "in steam" were of a lesser breed. As a matter of fact, "square rigged" ancient mariners are becoming rarer with the effluxion of time.

An outline of Robert Scot Skirving's career has been given—much has necessarily been omitted—but an attempt must be made to draw a composite picture of him. He had two major loves—the first was the sea, and it was always his greatest love; the other was medicine. Not far behind in third place came literature and the arts. Even when he travelled "in sail" he used to read Shakespeare

with his fellow apprentices. And it will be remembered that he used, in his parting lecture to his students, to advise them to read three books—Hilton's "Rest and Pain", the "Life of Sir James Paget" and the Bible. He insisted that to be a good doctor one ought to try to become an educated man. Many of his good qualities have been mentioned; to the casual acquaintance he might sometimes have appeared intolerant. On these occasions he chose his language from Holy Writ (as he used to call it), but used often to add expletives that came from his sailoring days. He seemed to enjoy the violence of his expressions, but a twinkle could always be detected in his eye—he had no malice. As a *raconteur* he was unequalled, and he told his stories with a kind of boyish relish; many of the stories, being true, showed what a shrewd judge he was of human nature. He was invariably kind to young people, even to the end of his days. It was given to few to know the real man behind the mosaic-like façade. We gain some insight from the way in which he planned his own funeral service. His coffin was covered with the red ensign of the Merchant Service and his wife's ashes in a casket were placed with flowers on the flag. He chose two hymns: "O God, our help in ages past" and "O love that wilt not let me go". He asked that Dr. George Bell should give the address. He used to say, quoting part of the eighth verse of the sixth

chapter of the Prophet Micah, that the duty of man was "to do justly, to love mercy, and to walk humbly with thy God". We know that he tried to do his duty and we may be thankful for the wide and beneficent influence that he had on men in all walks of life.

DR. DOUGLAS MILLER writes: He was very old, "far too old and too tired", according to himself, but for all that so much more alive than many who were by decades his juniors. He loved the English language and its poetry, the sea and its little ships, the world and its great men, in spite of frequent protestations that the Almighty made a great mistake in giving man such prominence in His scheme. I once told a very religious woman friend of Scot Skirving's that he had made some such remark. She told me later that she had challenged and chided him for accusing God of a mistake. "My dear", he said, "I should have called it a regrettable indiscretion." He had a tongue which could use the whole range of language and to which he could lend the beautiful sonorousness of his voice in healthy contumely and abuse of those who did not measure up to his standards, but he would thrill at a passing procession of soldiers and exclaim with proper pride: "We are a great people."

Long before I knew him I had in boyhood often heard of great kindness he had shown my uncle who had in years gone by been his house surgeon. This was a thoughtfulness and kindliness he exercised throughout his life.

When I was a student, I remember going with Sir Alexander MacCormick to Saint Vincent's Hospital and finding the sister-in-charge of the operating theatre in tears. "Dr. Scot Skirving did his last operation this morning", she said by way of excuse. MacCormick, who knew him so well, and had so little of the poetic or histrionic himself, commented on how he could appreciate the pathos with which Scot Skirving would invest this occasion.

"The trouble with MacCormick is that he has no poetry in his soul", I have often heard Skirving say, and MacCormick, not appreciating the place of poetry in medicine, always said: "Skirving should have been a parson. He was a great loss to the church."

Slowly he had to curtail his activities, and it is some years since the familiar red sails of his yacht were seen on the harbour, or since he would attend public functions, but he never restricted his intellectual activity or his avid interest in medicine. It fascinated him to see a pituitary adenoma operated on, and he waxed ecstatic over the very idea of cardiac surgery.

Until very recently he would often be seen sitting near the exit at professional meetings and lectures, of which he was always a direct and helpful critic, and was ready enough to make his views known. After a very long oration to which we listened one night, he said of the speaker with some suitable expletives: "He used all time and encroached on eternity." I remember, too, being sent for by him the day after I had lectured about something, and how he upbraided me for not using notes, for without notes, "how can anyone tell when the thing is going to end".

What generations of doctors are in his debt for his dramatic teaching, but much more so for his example and leadership in how to be a great doctor, an eager friend, and a kind and good man!

During a very recent visit he showed me current correspondence with Robert Hutchison, in which Hutchison protested his inability to keep up with modern progress and to answer some questions of Skirving's; and then we got off that subject, and as he led me to the door with all his courtly friendliness, he held me and recited a lovely reverberating passage from the Dante "Inferno". It was for me good-bye to a loved and honoured master and leader.

DR. J. G. EDWARDS writes: I have known the late Robert Scot Skirving since my student days at the Prince Alfred Hospital in 1905. In my early days of practice he often gave me most valuable advice, and since my move to Craignish in 1918 I have had the honour and pleasure of seeing him daily and of discussing many topics of interest. He was possessed of a unique personality and had a profound knowledge of all subjects both general and medical. He was an avid reader of old and modern literature and quoted frequently from the Bible and Shakespeare. He even enjoyed the modern detective stories. He had a deep knowledge of human nature and was never harsh in criticism of his contemporaries. He might pretend hatred for some individual, but always with a twinkle in his eye, and I think real hatred was foreign to him. He often spoke of death without fear, and his wife once told me that he took a book on his honeymoon entitled "Thoughts on Death and Other Poems".

He had a wonderful gift of language, and his students would often quote verbatim some of his utterances when lecturing on clinical medicine. His bedside lectures were a pleasure. He told me he always modelled his lectures on those of his old teacher Byrom Bramwell. He served in the Boer War and in the first World War.

He was always amused at being mistaken for Henry Irving and Bland Holt. On one occasion he ran for a cab in London, but was beaten to it by two inebriated Diggers. One of them looked at him and exclaimed: "Good Lord! If it ain't Bland Holt!"

In his youth he went to sea in sailing ships and gained his master's certificate, and on one of his voyages he visited Australia. This helped to decide him to come to Australia after graduation. He often wondered why he took to medicine, as his parents cultivated the land in southern Scotland and were noted horse breeders. When he decided to leave Edinburgh, Argyll Robertson tried to dissuade him and offered to take him into practice as an assistant. However, Skirving had made up his mind, and on leaving Edinburgh, Argyll Robertson presented him with an ivory handled set of eye instruments. This was a most prized possession.

He was the oldest medical graduate of the University of Edinburgh, and on each birthday anniversary the Senate sent him a cable of greeting. All the notable medical men who have visited this country in recent years called on him and he enjoyed these meetings.

When Scot Skirving arrived in Australia he intended to take up country practice, and while "prospecting" in Queensland Professor Thomas Anderson Stuart telegraphed him to come to Sydney and take over the superintendency of Prince Alfred Hospital.

As a surgeon he was a first class operator and as a consultant he was without equal. His very presence in a sick room brought hope and comfort to the most desperately ill. He was very fond of sailing boats, and it was a great grief to him when eighty that he could no longer climb a mast to fix the rigging. He always amused me in his latter years when he had to buy new clothes. He grumbled that he would not live to wear them out. He deplored the advent of the internal combustion engine, considering that it took so much of the picturesque out of life. Until his death he read his medical journals from cover to cover, and he could discuss all modern advances in medicine as keenly as if he was a recent graduate. He attended frequently at operations for complicated cardiac conditions, and only a few months before his death he stood for hours watching a resection of the abdominal aorta at Sydney Hospital.

Anecdotes of this great man are legion, and I could fill a book with stories he has told me and with stories I have heard from his contemporaries. And now he is no more. For nearly fifty years I have been his most intimate friend, and no one will miss him more than I.

DR. E. P. DARK writes: Even if it could not be said of Robert Scot Skirving that he had taken "all knowledge to be his province", we may wonder where we can find, in these times, a man with such a wide range of knowledge and such diversified skills—consulting surgeon and consulting physician; master mariner and novelist; deeply learned in art, literature and history; a great teacher and a superlative *raconteur*; as a trifling last, the writer of a small textbook on splicing, which not so long ago was still being reprinted for teaching budding mariners.

Towards the end of the first World War, after a sick leave, I travelled back to England with him, and had much kindness from him. I had thought myself fairly well educated, but soon realized that I knew nothing when he talked of history or literature.

We stayed together in New York, while waiting for a ship, and one afternoon looked through an art gallery; as we were strolling through one of the rooms he glanced across at a portrait hanging on the opposite wall. After a moment's study, he remarked: "That will be a Lely; about 1642."

Soon after the first examination for the Sydney M.S. was held, he told me with sardonic mirth how one of the young aspirants had asked for a cystocope for the diagnosis of a *tabes dorsalis* that had all the typical clinical signs. "Of course, I failed him", finished Scot Skirving with grim relish.

His biography should be made compulsory reading for all young graduates; it might persuade some of them that life is greater than medicine, and that in medicine one should rely first on one's clinical knowledge and one's trained senses, and only secondarily on gadgets, however marvellous.

How I wish I could hear his comment on the latest American device of diagnosis by slide rule!

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VERNARD FRANCIS ALOYSIUS O'NEILL.

DR. L. HALBERSTATER has sent the following appreciation of the late Dr. Vernard Francis Aloysius O'Neill.

Vernard Francis Aloysius O'Neill, M.B., Ch.M., died at Townsville on August 3, 1956, after a very short illness. He was born at Albury, New South Wales, sixty-three years ago. He attended the Fort Street High School and the Christian Brothers' College, Our Lady's Mount, Waverley, Sydney. From there he proceeded to St. John's College within the University of Sydney and graduated bachelor of medicine and master of surgery in 1917. He immediately joined the Australian Imperial Force. He was a medical officer at the Fourth Australian General Hospital in 1918 and 1919, and medical officer in charge of the Military Quarantine Station, North Head, Sydney, in 1919, as well as adviser to the Public Health Department, New South Wales, during the influenza epidemic, 1918-1919.

After his discharge from the Australian Imperial Force he was appointed medical superintendent of the Lewisham Public Hospital in Sydney. Then followed an appointment as assistant medical superintendent of the Newcastle Hospital, and in 1919 he proceeded to Charters Towers as medical superintendent. There he practised and built up a large surgical reputation. In 1925 he moved to Townsville, where he practised as a surgeon and radiologist until his death.

Whilst in Townsville he was an honorary medical officer of the Townsville Hospital from 1925 to 1937, when honorary service was abolished. He was a member of the Queensland Cancer Trust Treatment Clinic at the Townsville Hospital from 1931 to 1936, and was North Queensland delegate to the first Cancer Congress held in Canberra in 1931.

During the second World War he was Officer in Charge of the Surgical Division of the 16th Australian General Hospital in 1942, Deputy Assistant Director of Medical Services of the 2nd Lines of Communication Area, Kelvin Grove, from 1942 to 1944, and President of the Medical Board, Redbank, from 1944 to 1945, with the rank of lieutenant-colonel.

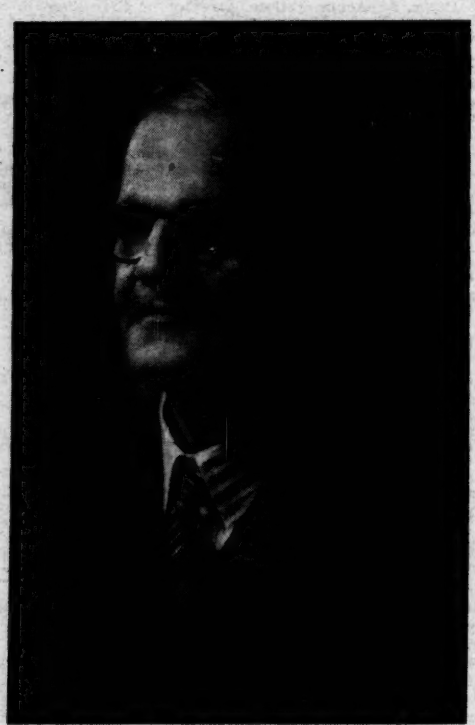
During his career in North Queensland he built up a reputation as a surgeon and radiologist which extended all over North Queensland. His health had not been good for the past fifteen years, but the end was very sudden and unexpected.

O'Neill was interested in art and had a large collection of Australian paintings of which he was a connoisseur. He was interested in racing for many years, both as an owner and breeder and on the administrative side, and won many important events on the turf in Brisbane and in North Queensland.

He is survived by a widow and three sons. All the sons are in the medical profession—namely, Dr. Vernard Francis (Bill) O'Neill, of Townsville, Dr. Brian O'Neill, of Inverell, New South Wales, and Dr. Gerald O'Neill, who is at present doing post-graduate work in England. He will be sadly missed by his colleagues, patients and friends.

EDWARD REGINALD ROW.

DR. EDWARD REGINALD ROW died peacefully in Brisbane on June 12, 1956, at the age of almost eighty-three years. He was born in Rockhampton, Queensland, on July 8, 1873. Both his parents were English. His father, Edward Rooke Row, was a chemist from Devonshire. His mother came from Walton, Staffordshire. As a small boy Reginald Row was sent to school in Hobart, and later to the Brisbane Grammar School, where he boarded from 1886 to 1891. His father died at an early age, so when he left school Reginald was apprenticed to his uncle, a chemist in Rockhampton. After a year of this he decided to become a doctor, and made arrangements to enrol at Guy's Hospital, London, where he commenced his medical course in 1894. While waiting for his ship in Brisbane he resided at Toowong, near the river, and so had an excellent view of the great flood of 1893. He well remembered rescuing people in a boat from the first floor of the Regatta Hotel.



Having taken his "conjoint" at Guy's, he returned to Queensland at the turn of the century in good time to sail again with the sixth Queensland Contingent for South Africa, where he served as a medical officer throughout the Boer War. After his return to Queensland he practised for a time at Nanango and at Thargomindah, leaving the latter township in 1907.

On June 18, 1908, he married Margaret Amelia Swift at Saint Michael and All Angels Church, New Farm, Brisbane. The following year the couple settled in Kilcoy, and commenced general practice. Kilcoy days were the most strenuous and the happiest of their lives. The period spent there till the end of 1923 saw the transition from horse and buggy to the motor-car. They also greeted the first railway train. Roads were few and bad in the district. Often the buggy had to be left behind and visits made on horseback.

Despite the demands of a busy and scattered country practice, Reginald Row took a keen interest in local affairs. He had much to do with the construction of the Kilcoy District Hospital, of which he was the first superintendent. In addition he served on the Shire Council and the local show society, and was a warden of Saint Mary's Church of England. When war commenced in 1914 he lost no time in joining the Australian Imperial Force. Unfortunately he was obliged to seek his release from service when on the

point of going abroad, as arrangements he had made for the care of his practice had proved unsatisfactory. This was the bitterest disappointment of his life. At the end of 1923 Dr. Row left Kilcoy and commenced practice in Brisbane, both in the suburb of Wilston and in the city.

In 1936 he moved towards retirement at Ashgrove, Brisbane, with the idea of seeing patients at Wickham Terrace only. However, the outbreak of World War II saw him working again as hard as ever, and it was not until 1948, or later, that he finally retired from practice.

The late Dr. E. R. Row was a conscientious family doctor, whose patients' welfare came first and foremost. He was invariably cheerful, was generous almost to a fault, and possessed a keen sense of humour, which did not desert him even at the end of his life. He found little spare time during his professional years for amusements or hobbies, but he was always very fond of games. He played in the first fifteen at the Brisbane Grammar School in 1890 and 1891, and stroked the crew in 1891. He continued to play Rugby while at Guy's Hospital and, in fact, followed London hospital Rugby with interest throughout his life. In 1942 he was elected President of the Brisbane Grammar School Old Boys' Association. Dr. Row leaves one daughter (Mrs. Athol Quayle) and three sons, two of whom are doctors.

Naval, Military and Air Force.

APPOINTMENTS.

THE undermentioned appointments, changes *et cetera* have been promulgated in the *Commonwealth of Australia Gazette*, Number 61, of October 25, 1956.

NAVAL FORCES OF THE COMMONWEALTH (SEA-GOING FORCES).

Termination of Appointment.—The appointment of Henry Macklin Ottway Brown as Surgeon Lieutenant (for Short Service) is terminated, dated 19th September, 1956.

AUSTRALIAN MILITARY FORCES.

The Australian Efficiency Decoration.

Lieutenant-Colonel S35727 Norman Stannus Gunning, Royal Australian Army Medical Corps (Medical) (now Retired List).

Citizen Military Forces.

Eastern Command.

Royal Australian Army Medical Corps (Medical).—2/235604 Honorary Captain D. P. Ewing is appointed from the Reserve of Officers, and to be Captain (provisionally), 22nd August, 1956.

Central Command.

Royal Australian Army Medical Corps (Medical).—4/32051 Captain (provisionally) R. G. Evans relinquishes the provisional rank of Captain, is transferred to the Reserve of Officers (Royal Australian Army Medical Corps (Medical)) (Central Command), and is granted the honorary rank of Captain, 5th August, 1956.

Western Command.

Royal Australian Army Medical Corps (Medical).—To be Temporary Major, 1st August, 1956: 5/26543 Captain J. M. McKenna.

Reserve Citizen Military Forces.

Royal Australian Army Medical Corps.

Northern Command.—The resignation of Honorary Captain P. B. Rowland of his commission is accepted, 4th July, 1956. To be Honorary Captains: Brian Timothy O'Sullivan, 7th September, 1956, and Noel Fredrick Langley and Miles Ellis Beirne Murphy, 10th September, 1956.

Eastern Command.—Honorary Captains W. M. Bevington and B. A. Stephen are retired, 14th February, 1956. The resignation of Honorary Captain B. Towers of his commission is accepted, 7th August, 1956. To be Honorary Captain, 13th September, 1956: William Colin Gale.

Southern Command.—Honorary Captain B. Cox is retired, 15th July, 1956.

DISEASES NOTIFIED IN EACH STATE AND TERRITORY OF AUSTRALIA FOR THE WEEK ENDED OCTOBER 20, 1956.[1]

Disease.	New South Wales.	Victoria.	Queensland.	South Australia.	Western Australia.	Tasmania.	Northern Territory.	Australian Capital Territory.	Australia.
Acute Rheumatism	3	5(2)	..	..	1	..	..	..	9
Amoebiasis	..	1(1)	..	..	..	..	..	..	1
Ancylostomiasis	..	..	181	..	..	..	..	..	181
Anthrax	..	..	1	..	..	..	..	..	1
Bilharziasis	..	..	..	..	..	..	..	..	..
Brucellosis	..	..	1	..	..	..	..	..	1
Cholera	..	..	..	..	..	..	..	..	..
Chorea (St. Vitus)	..	..	..	..	..	..	..	..	..
Dengue	..	..	..	..	..	..	..	..	..
Diarrhœa (Infantile)	1(1)	7(6)	1	..	..	..	1	2	12
Diphtheria	..	3(3)	..	..	1(1)	..	..	..	4
Dysentery (Bacillary)	..	4(3)	2(1)	..	..	..	..	..	6
Encephalitis	..	..	..	1(1)	..	..	..	..	1
Filariasis	..	..	..	..	..	..	..	..	..
Homologous Serum Jaundice	..	..	..	..	..	..	..	..	..
Hydatid	..	..	..	..	..	..	..	..	..
Infective Hepatitis	52(28)	38(17)	..	27(7)	2	4	3	5	131
Lead Poisoning	..	..	..	..	..	..	..	..	..
Leprosy	..	..	..	..	..	..	..	..	..
Leptospirosis	..	..	3	..	..	..	..	..	3
Malaria	..	..	..	..	..	..	..	..	..
Meningococcal Infection	1	5(4)	..	..	..	1	..	..	7
Ophthalmia	..	..	..	..	..	..	..	..	..
Ornithosis	..	..	..	..	..	..	..	..	..
Paratyphoid	..	..	..	..	..	..	..	..	..
Plague	..	..	..	..	..	..	..	..	..
Poliomyelitis	2(1)	..	1	4(3)	..	2(1)	..	..	9
Puerperal Fever	1(1)	..	..	..	..	..	..	..	1
Rubella	..	72(21)	1(1)	13(11)	1(1)	..	9	..	96
Salmonella Infection	..	..	..	..	1(1)	..	..	..	1
Scarlet Fever	11(7)	11(9)	10(2)	1	..	..	..	..	33
Smallpox	..	..	..	..	..	..	..	..	..
Tetanus	..	..	2(1)	..	..	..	..	..	2
Trachoma	..	..	..	..	..	..	11	..	11
Trichinosis	..	..	..	..	1(1)	..	..	..	1
Tuberculosis	36(27)	20(13)	8(4)	10(6)	15(8)	5(1)	..	..	94
Typhoid Fever	..	2(2)	..	..	..	..	..	..	2
Typhus (Flea-, Mite- and Tick-borne)	..	..	1	..	..	..	..	..	1
Typhus (Louse-borne)	..	..	..	..	..	..	..	..	..
Yellow Fever	..	..	..	..	..	..	..	..	..

[1] Figures in parentheses are those for the metropolitan area.

Central Command.—The following officers are retired, 15th February, 1956: Captain J. G. Woods and Honorary Captains T. D. Finey, R. O. Fox, W. E. George, M. E. H. Schafer and D. J. R. Sumner.

The following officers are placed upon the Retired List, with permission to retain their rank and wear the prescribed uniform:

Eastern Command. — Lieutenant-Colonel (Honorary Colonel) R. H. MacDonald, O.B.E., Lieutenant-Colonels R. V. Bretherton, L. F. Dods and I. D. Miller, Majors R. H. B. Bettington, S. V. Marshall, J. E. Traill and F. H. H. Wilson, and Captain G. J. Cuthbert, 14th February, 1956.

Central Command.—Major L. D. Cowling and Captain M. V. Samuel, 15th February, 1956.

Western Command.—Major B. St. P. Gillett, Captain (Honorary Major) C. W. Anderson, and Captain B. O. Bladen, 21st March, 1956.

The Royal Australasian College of Physicians.

EXAMINATION FOR MEMBERSHIP.

EXAMINATION for membership of The Royal Australasian College of Physicians will be held on the following dates in 1957:

First examination: Written examination (capital cities), Friday, April 12, 1957; clinical examination in Brisbane, commencing on or about Thursday, May 23, 1957; closing date for applications, Friday, March 15, 1957.

Second examination: Written examination (capital cities), Friday, August 30, 1957; clinical examination in Sydney, commencing on or about Thursday, October 10, 1957; closing date for applications, Friday, August 2, 1957.

Application forms may be obtained from the Honorary Secretary of the College, 145 Macquarie Street, Sydney.

ADMISSION OF MEMBERS.

AT a meeting of the Council of The Royal Australasian College of Physicians held in Melbourne on October 9, 1956, the following candidates, who were successful at an examination by the Australian Board of Censors, were admitted to membership of the College: Dr. A. G. Zaver, of Queensland; Dr. C. S. H. Reed, Dr. D. E. Smith and Dr. N. J. Yorkston, of New South Wales; Dr. C. W. Baird, Dr. R. H. D. Bean, Dr. J. L. Blunt, Dr. A. C. L. Clark, Dr. R. K. Doig and Dr. W. H. Orchard, of Victoria; Dr. N. D. Abbott, Dr. R. G. Gold and Dr. P. M. Last, of South Australia; Dr. D. D. Letham, of Western Australia.

Notice.

AUSTRALIAN CONGRESS OF PHYSICAL MEDICINE.

THE following is the programme of the eleventh Australian Congress of Physical Medicine to be held in Melbourne from November 12 to 14, 1956. Unless otherwise stated, all meetings will be held at the Royal Melbourne Hospital.

Monday, November 12: 9.15 a.m., Dr. M. Brous, "Acetylation and Methylation Disorders in Arthritis"; 11 a.m., Dr. Naomi Wing, "Modern Thought on Lesions of the Shoulder Region"; 2 p.m., "Coonac" Rehabilitation Centre; 8 p.m., Dr. Howard Rusk, a lecture at the Public Lecture Hall, University of Melbourne.

Tuesday, November 13: 9.15 a.m., Dr. R. Meyers, "Aspects of Rehabilitation"; 11 a.m., Dr. S. Nelson, "Trends in Research in the Rheumatic Diseases"; 2 p.m., Dr. L. Parr, "Antimalarial Treatment in Rheumatoid"; 3.30 p.m., Mr. C. Hembrow, "Some Aspects of Backache"; 8 p.m., Dr. F. Drew, "The Allergic Aspects of Rheumatic Disease", at the Medical Society Hall, 426 Albert Street, East Melbourne.

Wednesday, November 14: 9.15 a.m., Dr. F. May and Dr. L. Koadlow, clinical cases; 2.30 p.m., Dr. L. Wedlick, "Physical Medicine Overseas"; 4.30 p.m., annual meeting; 6.30 p.m., Association dinner, Union House, University of Melbourne.

Deaths.

THE following deaths have been announced:

FEATHERSTONE.—Frank Reginald Featherstone, on October 22, 1956, at Newport, New South Wales.

EAMES.—William L'Estrange Eames, on October 26, 1956, at Sydney.

Diary for the Month.

Nov. 12.—Western Australian Branch, B.M.A.: General Meeting.
Nov. 13.—New South Wales Branch, B.M.A.: Executive and Finance Committee.
Nov. 14.—Victorian Branch, B.M.A.: Branch Meeting.
Nov. 19.—Victorian Branch, B.M.A.: Finance Subcommittee.
Nov. 20.—New South Wales Branch, B.M.A.: Medical Politics Committee.
Nov. 22.—Victorian Branch, B.M.A.: Executive of Branch Council.

Medical Appointments: Important Notice.

MEDICAL PRACTITIONERS are requested not to apply for any appointment mentioned below without having first communicated with the Honorary Secretary of the Branch concerned, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

New South Wales Branch (Medical Secretary, 135 Macquarie Street, Sydney): All contract practice appointments in New South Wales.

Queensland Branch (Honorary Secretary, B.M.A. House, 225 Wickham Terrace, Brisbane, B17): Bundaberg Medical Institute. Members accepting LODGE appointments and those desiring to accept appointments to any COUNTRY HOSPITAL or position outside Australia are advised, in their own interests, to submit a copy of their Agreement to the Council before signing.

South Australian Branch (Honorary Secretary, 80 Brougham Place, North Adelaide): All contract practice appointments in South Australia.

Editorial Notices.

MANUSCRIPTS forwarded to the office of this journal cannot under any circumstances be returned. Original articles forwarded for publication are understood to be offered to THE MEDICAL JOURNAL OF AUSTRALIA alone, unless the contrary be stated.

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